Health-related quality of life in Indonesian children, adolescents, and adult patients with disorders of sex development

by Achmad Zulfa Juniarto

Disorders of sex development in Indonesia:

The course of psychological development in late identified patients

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Stoornissen van seksontwikkeling in Indonesië:
Psychologische ontwikkeling in patiënten bij wie
op latere leeftijd een diagnose is gesteld

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For my family and Raja

Chapter 1

General introduction

General introduction

In individuals with a disorder of sex development (DSD), prenatal development into male or female has deviated. As a consequence, a child is born with anomalies of the genital tract and may have ambiguous sex characteristics. In addition to genetics, steroid hormones plays an important role in sex development. Steroids are particularly important in the development of psychological aspects of gender. Ambiguity in body or behavior is rare and confrontation with a person who raises doubt about his or her gender often leads to confusion. A DSD condition therefore makes patients vulnerable for stigmatization.

In Western patients with DSD, diagnostic work-up and treatment follows immediately after identification of DSD. Medical treatments are given to prevent life-threatening consequences of the disorder and progressive genital and body masculinization in children raised as girls or development of female characteristics in adolescents raised as boys. Psychological counseling is offered to help parents cope with their emotions and problems met in daily life. An important aspect of the offered medical and psychological help is to prevent stigmatization and to provide optimal social opportunities. This policy has been developed 50 years ago.

During the past 20 years, there has been a debate about the advantages and disadvantages of this policy of early interventions in children with DSD. These critics mainly focus on the fact that many decisions taken brought enormous impact on the future lives of these children whereas children are often too young to be involved in the decision making. In non-Western countries, doctors mostly see patients who seek medical care later in life. Many patients and parents will only consult a doctor after psychological or social problems with genital or body ambiguity have intensified. In Indonesia, DSD is not known widely; treatments are available in six type-A hospitals, medical professionals with expertise on DSD are very rare, and medical treatments are expensive. Delay of treatment allowed us to study the course of psychological development in patients with DSD who, for a long time, did not receive medical attention and the implications on gender development and psychosocial adaptation. To date, no such study had been done before in Indonesia, while such a study is almost impossible to achieve in Western countries.

This study is part of a clinical study on etiology and management of DSD in a large group of undiagnosed and untreated DSD patients in Semarang, Indonesia. It focuses on the psychosexual development and psychological wellbeing aspects in these patients: body image, sexual functioning, sexual orientation, gender development, emotional and behavioral problem, social stigmatization, and health-related quality of life. Findings from both studies will be used to develop a clinical guideline for providing an integrated treatment plan for our patients with DSD.

What is DSD?

Disorders of sex development (DSD) is an umbrella term covering congenital conditions in which the development of chromosome, gonads, internal and external genitalia did not follow the normal path of male or female (Hughes, Houk, Ahmed, & Lee, 2006). As DSD covers a broad range of sex anomalies, a new classification of DSD diagnoses had been proposed in the Chicago consensus which classified all DSD condition into three groups: a) 46,XX DSD; b) 46,XY DSD; and c) sex chromosome DSD (Hughes et al, 2006).

The three most common causes of DSD are: congenital adrenal hyperplasia (CAH), androgen insensitivity syndrome (AIS), and mixed gonadal dysgenesis (Hewitt & Warne, 2009). Table 1 summarizes the DSD diagnoses by cause as proposed in the Chicago consensus conference (Hughes et al., 2006).

Table 1 Classification of disorders of sex development (DSD)

Sex chromosome DSD	46,XY DSD	46,XX DSD
A: 47,XXY (Klinefelter syndrome and variants)	A: Disorders of gonadal (testicular) development 1. Complete or partial gonadal dysgenesis (e.g. SRY, SOX9, SF1, WT1, DHH etc) 2. Ovotesticular DSD 3. Testis regression	A: Disorders of gonadal (ovarian) development 1. Gonadal dysgenesis 2. Ovotesticular DSD 3. Testicular DSD (e.g. SRYþ, dup SOX9, RSP01)
B: 45,X (Turner syndrome and variants)	B: Disorders in androgen synthesis or action 1. Disorders of androgen synthesis LH receptor mutations Smithe-Lemlie-Opitz syndrome Steroidogenic acute regulatory protein mutations Cholesterol side-chain cleavage (CYP11A1) 3b-hydoxysteroid dehydrogenase 2 (HSD3B2) 17a-hydroxylase/17,20-lyase (CYP17) P450 oxidoreductase (POR) 17b-hydoxysteroid dehydrogenase (HSD17B3) 5a-reductase 2 (SRD5A2) 2. Disorders of androgen action Androgen Insensitivity Syndrome Drugs and environmental modulators	B: Androgen excess 1. Fetal 3b-hydoxysteroid dehydrogenase 2 HSD3B2 21-hydroxylase (CYP21A2) P450 oxidoreductase (POR) 11b-hydoxylase (CYP11B1) Glucocorticoid receptor mutations 2. Fetoplacental Aromatase (CYP19) deficiency Oxidoreductase (POR) deficiency 3. Maternal Maternal virilizing tumours (e.g. luteomas) Androgenic drugs
C: 45,X/46,XY (mixed gonadal dysgenesis)	C: Other 1. Syndromic associations of male genital development (e.g. cloacal anomalies, Robinow, Aarskog, Hand-Foot-Genital, popliteal pterygium) 2. Persistent Müllerian duct syndrome 3. Vanishing testis syndrome 4. Isolated hypospadias (CXorf6) 5. Congenital hypogonadotropic hypogonadism 6. Cryptorchidism (INSL3, GREAT) 7. Environmental influences Cloacal exstrophy	C: Other 1. Syndromic associations (e.g. cloacal anomalies) 2. Müllerian agenesis/ hypoplasia (e.g. MURCS) 3. Uterine abnormalities (e.g. MODY5) 4. Vaginal atresis (e.g. KcKusickeKaufman) 5. Labial adhesions Cloacal malformation Cloacal exstrophy
D: 46,XX/46,XY (chimerism)		

Source: Hughes, et al., 2006.

DSD and psychological consequences

The number of studies among individuals with DSD have been increased rapidly in the past decades, including the psychological field. Findings from previous psychological studies on patients with DSD, particularly diagnoses relevant to this study, will be summarized below.

46,XX Congenital adrenal hyperplasia (CAH)

CAH is an autosomal recessive disorder that mainly caused by the 21-hydroxylase enzyme deficiency (White & Speiser, 2000). This enzyme deficiency prohibits adrenals from producing cortisone and aldosterone from cortisol, consequently all cortisol will be metabolized into androgens. The excessive production of adrenal androgen will impact profoundly in female in which the body, and particularly external genitals, will be masculinized. In patients with a complete or nearly complete block of the 21-hydroxylase production, masculinization of the external genitals will be severe: a nearly normal male appearance at birth with a "penis" and an empty scrotum. In such newborn, a male gender may be assigned. In patients with an incomplete block of the 21-hydroxylase production, the masculinization of the external genitals will be less severe and will have an ambiguous appearance at birth (Hines, 2004). If left untreated, the adrenal glands will continue to produce large amounts of androgens and masculinization of the body will be progressive. In puberty, body masculinization will lead to a male appearance and failure in development of female characteristics or development of both male and female secondary sex characteristics (i.e. development of breasts as well as facial hair).

In Western countries, particularly countries that implement newborn screening for CAH, CAH can be identified soon after birth and therefore, medical treatment can be offered soon. These newborns will likely be raised as a girls, and will receive glucocorticoid treatment. It is chosen to raise these children as girls, as they have ovaries and a womb, and they are fertile as women but not as men. Parents will receive education about CAH, parenting of a child with CAH, and understanding the risks of CAH in the next pregnancy. However, different cultures might imposed different practices in gender assignment on newborn with an ambiguous genitalia. A newborn with 46,XX CAH might had been assigned male and raised as a boy (Lee, Houk, & Husmann, 2010), particularly when the affected individuals were referred late for identification (Sripathi et al., 1997; Julka, et al., 2006).

Gender identity, gender role behavior, gender dysphoria, sexual functioning, and sexual orientation had been the main focus of psychological research on patients with CAH (Stout, Litvak, Robbins, & Sandberg, 2010). Previous studies revealed that young girls with CAH behave more masculine than healthy girls (i.e. siblings, healthy control subjects), have fewer interests in feminine-type of activities and often prefer typically masculine-type of

activities (Beltz, Swanson, & Berenbaum, 2011; Berenbaum, Duck, & Bryk, 2000; Berenbaum & Hines, 1992; Berenbaum, Korman Bryk, Duck, & Resnick, 2004; Hines, Brook, & Conway, 2004). Girls born with more severe masculinization of the external genitalia displayed more masculine behaviors than girls who had milder genital masculinization at birth. It is assumed that severity of masculinization of the external genital at birth reflects the level of circulating prenatal androgens. Hence, there also seems to be a dose-effect of level of prenatal androgens on gender role behavior (Meyer-Bahlburg, Dolezal, Baker, Ehrhardt, & New, 2006). Another study revealed that parenting practice does not influence the development of masculine behavior in girls with 46,XX CAH (Pasterski, et al., 2005).

The prevalence of the social gender role change in adult women appears to be between 1.5 – 2%, which is higher than in the non-DSD population (Dessens, Slijper, & Drop, 2005), but not high enough to change the present practice of gender assignment, particularly not as there is no correlation found with neonatal genital masculinization.

Studies on sexual functioning in women with CAH reported some problems with sexual functioning and intimate relationships (Crouch, Liao, Woodhouse, Conway, & Creighton, 2008; Gastaud, et al., 2007; van der Zwan et al., 2012), whereas other studies reported satisfaction with sex life and no problem with sexual functioning after genital surgeries (Nordenström, et al., 2010).

Androgen insensitivity syndrome (AIS)

AIS is defined as a disorder resulting from complete or partial resistance to the actions of androgens in an XY individuals with normal testis determination and production of age-appropriate androgen concentrations (Hughes, et al., 2012). AIS is a genetic disorder, in which the affected XY individuals was inherited through the X-linked trait (Hines, 2004). Each cell contains the defective androgen receptor. As a consequence, the body is unable to response to testosterone and the body feminizes. The complete form of AIS (CAIS) is characterized by a female phenotype, while in the partial form of AIS (PAIS), the genitals appear ambiguous. Most individuals with CAIS are assigned female at birth. The disorder will become apparent in adolescence when menses stay out. A medical examination will reveal 46,XY karyotype, undescended testes, and no Müllerian structures (Hines, 2004).

The large majority of individuals with 46,XY CAIS develop a female gender identity and display feminine gender role behavior (Hines, Ahmed, & Hughes, 2003). The literature only comprises a few case reports of CAIS patients who developed a male gender identity (T'joen et al., 2011; Kulshreshtha et al., 2011). In contrasts, individuals with 46,XY PAIS will be raised as men or women. Studies on gender role behavior revealed that individuals with 46,XY PAIS raised as girls are more masculine in their behavior than healthy control girls, whereas individuals raised as boys prefer girls as their playmates compared to healthy boys who prefer male playmates only (Jürgensen, Hiort, Holterhus, & Thyen, 2007). Studies on gender identity revealed that gender dysphoria and social gender role change are seen in about 10% patients with PAIS (Mazur, 2005; Melo et al., 2003) either raised as females or males.

Review studies on the quality of life of women with 46,XY DSD revealed varying results: women with chromosomal male did not differ, or had better, or lower quality of life than the comparative groups assessed (Wisniewski & Mazur, 2005). Bouvattier and coworkers (2006) observed sexual functioning of adults with 46, XY PAIS raised as men. They reported sexual problems and impaired sexual functioning among this patient group.

Gonadal dysgenesis

Gonadal dysgenesis includes various clinical conditions characterized by an abnormal and underdevelopment of the fetal gonads. Complete gonadal dysgenesis in 46,XY individuals is characterized by a female phenotype with full development of the female genitals, normally developed Müllerian structures, and streak gonads. The affected individuals may not be identified until adolescence when the onset of puberty does not occur (Öcal, 2011). Serum FSH and LH levels are high, due to primary gonadal failure. Since women with this condition have a uterus, hormone replacement therapy is able to induce secondary sex characteristics including menses. As they have non-functional gonads, these women are infertile (Warne, 2008), but childbirth may be achieved through ovum donation and in vitro fertilization. Gonadal removal is usually performed in early life to anticipate the increased risk of malignancy. Individuals with a 46,XY complete gonadal dysgenesis are usually assigned female and identify themselves as females. Gender identity confusion or gender reassignment has not been reported among patients with gonadal dysgenesis (McCarty et al., 2008). A follow-up study of 19 adults with mixed

or partial gonadal dysgenesis raised as men or women observed that women reported more sexual problems than men (Szarras-Czapnik, Lew-Starowicz, & Zucker, 2007).

Sex chromosomal DSD

Sex chromosomal DSD includes the 45,X Turner Syndrome (TS) and variants; 47,XXY Klinefelter Syndrome (KS) and variants; 45,X/46,XY with mixed gonadal dysgenesis; and 46,XX/46,XY chimerism. Women with TS are phenotypically female and raised as girls (Lippe, 1991). Women with TS have full development of the external female genitalia, normally developed Müllerian structures, and streak gonads. There is considerable heterogeneity in dysmorphic body characteristics, health status, and neuropsychological functioning in women with TS (Rovet, 2004). Studies on gender role behavior and gender identity show that females with TS are typically female (Theilgaard, 1972; Money & Mittenthal, 1970; Downey et al., 1987, Collaer et al., 2002).

Men with KS are phenotypically male and raised as men (Aksglaede & Juul ,2013). Most men with KS have small testes, hypergonadotropic hypogonadism, and azoospermia in the majority of cases. There is large heterogeneity in dysmorphic body characteristics, health status, and neuropsychological functioning among men with KS (Groth et al., 2013). The large majority of men with KS have masculine gender identities, but in the last 45 years some cases of gender dysphoria and the wish for a gender role change have been reported (Hoaken, et al., 1964, Miller & Caplan, 1965; Davidson, 1966; Müller, 1972; Cryan & O'Donoghue, 1992; Seifert & Windgassen, 1995).

45,X/46,XY and mixed gonadal dysgenesis is associated with marked phenotypic variability, including females with Turner syndrome features, children with ambiguous genitals, and normal males (Telvi, Lebbar, Del Pino, Barbet, & Chaussain, 1999). There is also large variability in neuropsychological functioning but it seems that those children raised as girls are more affected than those children raised as boys (Tosson, Rose, & Gartner, 2012). Not much is known on the gender identity development in individuals with mixed gonadal dysgenesis. Only a few larger studies and several case studies have been published (Richter-Appelt et al., 2005; Migeon et al., 2002; Reiner, 2005; Warne et al., 2005; Reiner, 1996; Birnbacker et al., 1999; Ammini et al., 2002, Öcal, et al.,2012). These data indicate that about 30% of patients who had been raised as females made a social gender role change in adolescence.

Patients with different DSD diagnoses reported impaired body image, problems in establishing romantic relationships, and difficulties with sexual functioning (Bouvattier, Mignot, Lefèvre, Morel, & Bougnères, 2006; Crouch, Liao, Woodhouse, Conway, & Creighton, 2008; Gastaud et al., 2007; Kojima et al., 2009; Migeon et al., 2002; Minto, Liao, Conway, & Creighton, 2003; Szarras-Czapnik, Lew-Starowicz, & Zucker, 2007; Wisniewski et al., 2000).

Schützmann, Brinkmann, Schacht, and Richter-Appelt (2009) found that 59% of the adults with DSD reported severe psychological distress. However, a study on adolescents with DSD concluded that DSD does not impact their mental health (Kleinemeier, Jürgensen, Lux, Widenka, and Thyen, 2010). Gender differences in emotional and behavioral problem among patients with DSD are inconclusive. Zhu and colleagues (2010) observed more emotional and behavioral problems in boys with DSD than the matched controls, but this was not found among girls. Trautman, Meyer-Bahlburg, Postelnek, and New (1995) and Hirvikoski et al. (2008) did not find behavioral problems in girls with CAH, but Öner and colleagues (2011) observed more externalizing behavior and general behavioral problems in patients than in the control girls. Tosson, Rose, and Gartner (2012) observed that children with 45,X/46,XY raised as girls were more likely than those raised as boys to have behavioral problems. In contrast, a study on adolescent German girls with DSD aged 13-16 reported that these young patients did not differ from the control girls in terms of quality of life (Kleinemeier, et al., 2010).

Gender and gender variance in Indonesian socio-cultural context

Indonesia is a country of over 237 million people with a large cultural and religious diversity: 300 native ethnicities, 724 local languages and dialects, and five religions (Islam, Roman Catholic, Protestan, Hindu, and Buddha). Javanese is the major ethnic group and Java island is the most populous island in Indonesia. *Bahasa Indonesia* is the national language used throughout the country and taught during formal education (schools).

In order to obtain citizenship, every newborn must be registered, as male or female, within 60 days after birth, also in case of genital ambiguity. A birth certificate is compulsory for school entry, and for obtaining a diploma, health insurance, and an ID card. Delayed birth registration or change of gender in the birth registry requires a legal procedure in an Indonesian state court. In case a gender change is requested, the court will request a medical review

before reaching a decision. Gender change for patients with DSD received support from the Indonesian Moslem clerics (Haryadi, 2010). DSD is not widely known among general population in Indonesia, and not even among many health practitioners. Moreover, knowledge about DSD was limited until the last decade when education about DSD and genetic counseling was initiated by the Faculty of Medicine, Diponegoro University (FMDU). However, in the general population of Indonesia, the term "hermaphrodite" is known and often perceived by mistake as persons with double genitals (in *Bahasa: "kelamin ganda"*).

Gender variances and transgenderism is known in Indonesia. Persons with transgender are called *waria* or *banci* (in *Bahasa*) or *bencong* or *wandu* (Javanese). In daily live, girls who present themselves (with clothing, haircut, or behavior) in a masculine way are called *tomboi* (Blackwood, 2005). Transgender persons as well as gay men or lesbian women are not socially accepted, although their presence is known (Vaswani, 2010). In Indonesia, the term "homosexuality" is strongly associated with sin (Boellstorff, 2004). An anthropological study reported on *Bissu* in the Sulawesi, traditional priests believed to have both male and female characteristics (Graham, 2009). However, it seems that nowadays this Bissu cult is not practiced anymore. At least, this Sulawesian folklore is not well-known to the general population of Indonesia. Among the traditional Javanese puppets ('*wayang*') based on the Javanese Mahabarata, there is one figure that represents gender change, so-called *Srikandhi*. *Srikandhi* represents a female figure who has masculine traits and is represented as a female warrior or fighter (Sunindyo, 1998). The name or symbol *Srikandhi* has been used often by non-government initiatives, particularly in the field of women empowerment. This may suggests that masculinity in women is socially accepted in Javanese folklore.

In Indonesian society, marriage is a precondition for becoming a fully respected member of society and being unmarried, particular for women, is considered to bring shame to the family (Mulder, 1992). Shame (in Javanese: *'isin'*) is a fundamental element in Javanese culture and is taught from early childhood onwards (Keeler, 1983). When Indonesian adolescents enter adulthood, the social expectancies with respect to marriage and kinship and other social responsibilities will be intensified. Javanese people have been thought, since early life, to follow social norms and to ensure that social relations are in harmony.

Management of DSD in Indonesia

The government of Indonesian had appointed six state hospitals to provide medical treatment for patients with genital anomalies. The Sexual Adjustment Team/SAT *("Tim Penyesuaian Kelamin")* was established in 1989 in collaboration between the Dr Kariadi Hospital and the Faculty of Medicine of the Diponegoro University (FMDU) in Semarang, Central Java. Over the years, this team expanded. At present the multidisciplinary team includes many specialties, including pediatric, endocrinology, urology, andrology, obstetrics and gynecology, genetics, radiology, pathology, plastic surgery, psychology, psychiatry, social services, law and ethics.

Over the times, the SAT had been challenged mainly by the limited resources for diagnostic procedure and treatment. As a type A hospital in Central Java, the dr Kariadi Hospital receives referral particularly from poor people. The Indonesian government does provide universal health insurance called the Health Insurance Scheme for the Population, *('Jaminan Kesehatan Masyarakat'* or *'Jamkesmas')*, which aims to provide free health care services for common disease, including antenatal, delivery, or postnatal care services for mothers and infants (Ministry of Health Republic of Indonesia - The Directorate General of Community Health, 2008; Rokx, Schieber, Harimurti, Tandon, & Somanathan, 2009). However, this insurance policy was not widely known among poor people (Titaley, Hunter, Dibley, & Heywood, 2010), and does not cover hormonal and genetic tests. As a consequence, poor people often have to use their out of their own pocket money for obtaining medical treatment (Chee, Borowitz, & Barraclough, 2009), including our patients with DSD.

In 2004, an international collaboration was initiated by Prof. dr. Sultana M.H. Farads, MD, PhD (geneticist and coordinator of the SAT) and Prof. dr. S.L.S Drop, MD, PhD (pediatric endocrinologist and coordinator of the DSD team in the ErasmusMC-Sophia, Rotterdam) to improve our expertise through research and academic activities in the DSD field. Within this international collaboration, several seminars, workshops and teaching sessions were organized to increase awareness and expertise in management of DSD among Indonesian medical professionals. Between 1989 and 2010, 589 patients had been referred to SAT, in which 347 patients were evaluated clinically. Following the inclusion criteria applied for the study, 286 patients were included in the clinical study, and 118 were enrolled in the psychological study.

Aims of the study

This study was designed to give a comprehensive description on the psychological condition of patients with DSD in comparison with the matched control subjects. For the majority of these patients, diagnostic procedures were performed later in life and in some patients, treatment was initiated. Consequently, many patients had lived without treatment, in ambiguous bodies and gender, for most of their lives. In the Netherlands as well as most Western countries, diagnostic procedures and treatment start immediately following the identification of DSD.

This psychological study investigated gender identity, gender role behavior, body image, sexual functioning, sexual orientation, emotional and behavioral problems, social stigmatization, and health-related quality of life of children, adolescents, and adult patients with DSD in Semarang, Indonesia.

Outline of the thesis

Chapter 2 provides general information about the method of this cross-sectional study, which are not explained in detail in the following chapters, such as scale construction and validation and methodological challenges in conducting a case-control psychological study in Indonesia.

In chapter 3, findings from the study on body image and sexuality among 34 adult patients with DSD are reported. Sexuality, in this study, refers to male and female sexual functioning, female sexual distress, and sexual orientation.

Chapter 4 comprises a unique study on gender development among 60 children, 24 adolescents, and 34 adult patients with DSD. In this study, gender identity confusion and gender role behavior as well as satisfaction with the assigned gender are investigated. In addition to findings from the patient-matched control comparisons, we report findings on gender development among patients across DSD diagnoses. Furthermore we provide an evaluation on the gender development of patients who had changed their social gender role before entering medical service or patients who reported gender confusion at the time of study.

In chapter 5, we present our findings from a study on emotional and behavioral problems in patients with DSD. We identified different types of emotional and behavioral problems reported among patients and the percentage of patients with DSD who scored within the borderline range of emotional problems. More patients with DSD suffered from emotional and behavioral problems.

In chapter 6, we report on patients' experiences with social stigmatization. This study is relevant as for many years, early medical intervention in young patients with DSD had been under debate for its purpose of preventing stigmatization in later life but in fact, a systematic study on DSD patients' experiences with stigmatization is still lacking in the literature. In this study, quantitative and qualitative methods were applied in order to obtain insight in severity of stigmatization and the associated experienced distress. Qualitative data are used in addition to quantitative data obtained from measures developed specifically for the study of social stigmatization in patients and parents of youngsters with DSD.

In chapter 7, we describe our findings from a study on the health-related quality of life in patients with DSD. We compared the health-related quality of life in children, adolescents, and adult patients to their matched controls to find out to what extent the patients' quality of life was impaired.

In chapter 8, the findings from these five studies are discussed in broader context. Implications for future studies as well as for management of patients with DSD in Indonesia will be presented.

Chapter 9 contains a summary of findings from all studies reported above.

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Chapter 2

Methods of study

Methods of study

This chapter provides methodological details that are not described in the following chapters.

Study Design

This study is a unique investigation of the psychological development of Indonesian patients with DSD who had been referred to the Sexual Adjustment Team (SAT) of the Dr. Kariadi Hospital and the Faculty of Medicine, Diponegoro University (FMDU), Semarang, Indonesia for medical treatment. Before entrance, the majority of these patients had received little medical attention.

In the studies presented in Chapter 3, 4, 5, and 7, we compared patients with DSD to the healthy control subjects matched for gender, age, and residential setting (urban, suburban, rural) on the psychosexual development and psychological well-being.

As no Indonesian instruments were available to measure these constructs, instruments developed in Western countries were selected and translated for the Indonesian population. Application of internationally recognized measures in similar studies allow comparison between findings by other researchers and findings from Indonesian study. International comparison is valuable as it can give insight in cultural factors that play a role in the psychological aspects of DSD. We selected instruments based on two criteria: 1) the original version has good psychometric qualities, and 2) the measure has been used in previous studies in patients with DSD. Translated questionnaires may not have the same psychometric properties in the different language and culture they are introduced. Therefore, validity and reliability of the translated questionnaires need to be investigated. The procedures followed are described under Study preparation.

Study preparation: Scale adaptation/construction

Procedure

The scale adaptation procedures applied is illustrated in Figure 1. Translation of questionnaires was performed by certified translators from The Language Academy of the University of Amsterdam, the Netherlands (UVA Talen). For copy-righted questionnaires, translations rights were obtained. Prior to implementation, the Indonesian versions of the measurements were reviewed by the researcher (AE) and a Dutch anthropologist (Dr Saskia E. Wieringa) who is well-understood Indonesian culture, customs, and language, followed by an initial trial in healthy subjects. A few minor adaptations were made. Details can be found in the chapters 3-7.

Method

To assess the validity and reliability of adapted measures, we collected data through three different methods of survey: a) web-based survey, b) school-based survey, and c) face-to-face interview.

Web-based survey. Internet survey enables participation of a large sample of Indonesian adults, aged 18 years or older, across different provinces in Indonesia in a short period of time. Internet connection and familiarity with electronic surveys are required from potential respondents. We propagated our survey using mailing-lists and a Facebook page and reached well educated adults, aged 18-45 years. Details about this survey are provided in chapters 3 and 4.

School-based survey. The aim of this survey is to recruit a large sample of students from elementary schools, junior and senior high schools colleges and universities in Central Java and Yogyakarta provinces to fill out questionnaires as a paper-and-pencil test. Ten schools and four universities in Central Java and Yogyakarta provinces participated. Details about this survey can be found in chapters 5 and 7.

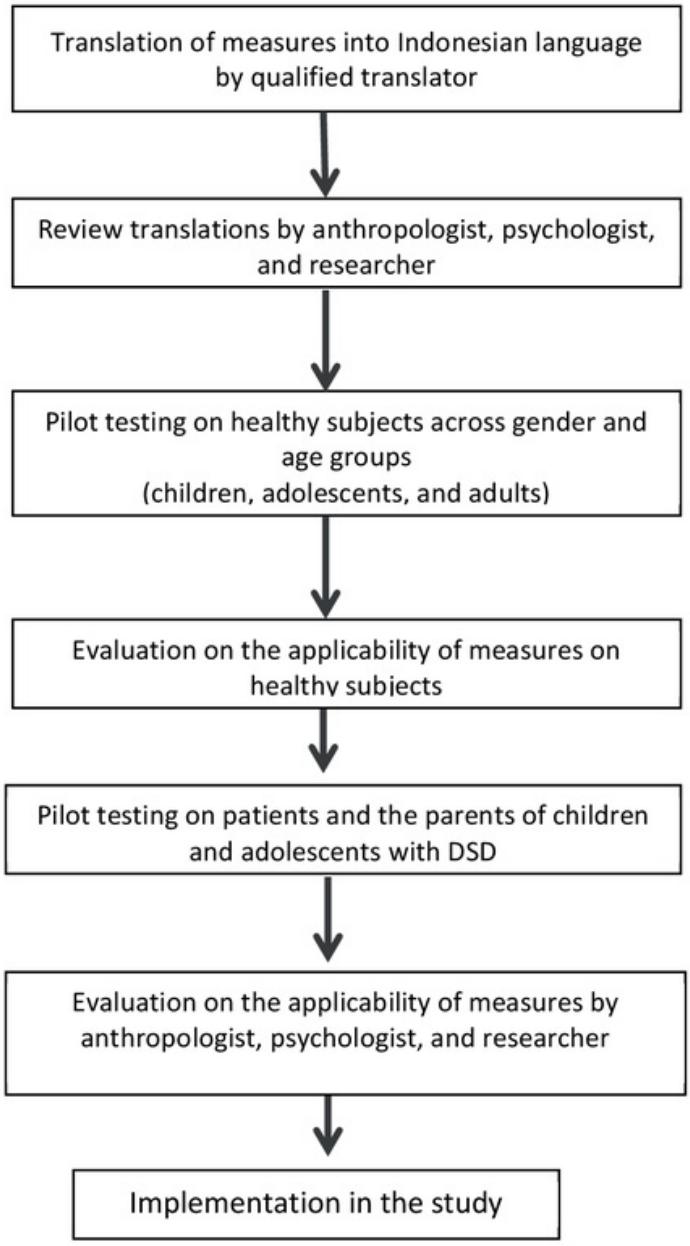

Figure 1. Procedures on adaptation of measures applied in the study

Face-to-face interview. Semi-structured interviews combines the opportunity of elaborative answers and quantitative measures. Elaborative answers were required in investigations in gender identity and social stigma. Detailed information can be found in chapters 4 and 6).

Measures

Table 1 summarizes the measures applied in the study, number of participants enrolled to assess validity and reliability of measures, and method applied to collect study participants. Detailed information on the validity and reliability of measures can be found in chapters 3-7.

Participants

To assess the psychometric properties of our measures, 5024 participants volunteered: 240 children and 245 parents, 1534 adolescents, and 3005 adults. See Table 1 for the number of participants based on the methods applied in the study and the relevant chapters discuss in details.

Statistical analysis for assessing validity and reliability of measures

In order to be able to compare data internationally, we followed methods in accordance with the method applied by the authors of the original scales. The principal component analysis was used to assess the factor structure of measure, whereas reliability was assessed using the internal consistency which was measured by the Cronbach's alpha. Detailed information on the applied procedures can be found in the chapter 3-7 as well as the psychometric properties of the applied measures.

Studies in patients with DSD

Participants

We eventually included 118 patients with a DSD condition, aged 6-41 years, and 118 healthy control subjects matched for age, gender, and residential setting (living in rural, suburban, or urban area).

Patients with DSD.

Inclusion criteria

Individuals with DSD aged 6 or older. Patients with the following diagnosis were included:

I. 46,XY DSD. Clinically the patients presented with underdeveloped or ambiguous external and/or internal genitalia

Table 1 Measures translated into Indonesian language, number of participants, and method used for scale validation

Instruments and reference	Outcome measure	Target population	Web-based survey (*n*)	School-based survey (*n*)	Individual interview (*n*)	Chapters
Body Image Scale (Lindgren & Pauly, 1975)	Body image and satisfaction	Adults aged 18 or older	243	n.a.	n.a.	3
Female Sexual Dissatisfaction Scale – Revised/FSDS-R (DeRogatis, Clayton, Lewis-D'Agostino, Wunderlich, & Fu, 2008)	Female sexual distress	Adults aged 18 or older	185	n.a.	n.a.	3
Female Sexual Functioning Index/FSFI (Rosen, 2002)	Female sexual functioning	Adults aged 18 or older	94	n.a.	n.a.	3
Kinsey Heterosexual-Homosexual Rating Scale (Kinsey, Pomeroy, & Martin, 1948; 1953)	Sexual orientation	Adults aged 18 or older	210	n.a.	n.a.	3
Male Sexual Health Questionnaire/MSHQ (Rosen, et al., 2004)	Male sexual functioning	Adults aged 18 or older	41	n.a.	n.a.	3
Activities Questionnaire (Hines, Ahmed, & Hughes, 2003)	Gender role behavior	Adolescents or adults aged 12 or older	254	n.a.	48 [a]	4
Gender Identity interview for children/GIIC (Zucker & Bradley, 1995)	Gender identity confusion	Children aged 6-11	n.a.	n.a.	120 [a]	4
Gender Identity Questionnaire for Children/GIQC (Cohen-Kettenis, et al., 2006)	Gender role behavior	Parents of children aged 6-11	n.a.	n.a.	120 [a]	4
Gender Questionnaire (Hines, et al., 2003)	Gender identity	Adolescents or adults aged 12 or older	316	n.a.	48 [a]	4
Adult Self Report/ ASR (aged 18-59) (Achenbach & Rescorla, 2001)	Emotional and behavioral problems	Adults aged 18 or older	n.a.	1091	n.a.	5
Child Behavior Checklist /CBCL 6-18 (Achenbach & Rescorla, 2001)	Emotional and behavioral problems	Parents of children aged 6-11	n.a.	n.a.	107	5
Youth Self Report/YSR (Achenbach & Rescorla, 2001)	Emotional and behavioral problems	Adolescents aged 12-15	n.a.	1154	n.a.	5

Instruments and reference	Outcome measure	Target population	Web-based survey (*n*)	School-based survey (*n*)	Individual interview (*n*)	Chapters
Social stigmatization scale on DSD – Parent report	Social Stigmatization [b]	Parents of patients aged 6-17 years	n.a.	n.a.	81 [c]	6
Social stigmatization scale on DSD – Adult report	Social Stigmatization [b]	Adults aged 18 or older	n.a.	n.a.	34 [c]	6
TACQOL PF 6-15 (Verrips, et al., 1999)	Health-related quality of life (generic)	Parents of children aged 6-15	n.a.	n.a.	57	7
TACQOL CF 8-15 (Verrips, et al., 1999)	Health-related quality of life (generic)	Children aged 8-15	n.a.	284	n.a.	7
TAAQOL (aged 16 year or older) (Verrips, et al., 1999)	Health-related quality of life (generic)	Adults aged 16 or older	n.a.	326	n.a.	7

[a] The participants comprised patients and matched control subjects; [b] The measure was developed specific for the study; [c] The participants comprised patients and parents of children and adolescents

a. Androgen Action Disorder. This group comprises patients with complete and partial androgen insensitivity syndromes (CAIS, PAIS). In these patients, testes are present but may be undescended uni-or bilaterally. Hormonal testicular function is normal but androgen action is presumed not to be fully effective. Ultimate proof is the demonstration of a mutation in the androgen receptor gene. In the absence of an AR gene mutation, the following criteria applied:
    - Pre pubertal age (0-12 years): No evidence of impaired action of androgens except in the infant 2-4 months with elevated serum levels of luteinizing hormone, follicle stimulating hormone, and testosterone (mini puberty condition).
    - Post Pubertal age (after 12 years): Serum levels of luteinizing hormone, testosterone, and anti-müllerian hormone are elevated.

b. Gonadal dysgenesis: This group comprises patients with underdeveloped testes and / or testes that cannot produce normal levels of steroids. Therefore

serum levels of luteinizing hormone, follicle stimulating hormone are high, of anti-müllerian hormone/Inhibin are low. The testosterone response in the human chorionic gonadotropin (HCG/Pregnyl) test is insufficient.

c. Under masculinization of unknown cause: This group comprises patients with underdeveloped external genitalia but with descended testes and normal internal male development in whom no cause for underdevelopment /under masculinization could be identified. Serum hormone values and response to HCG/Pregnyl are all normal for age.

.

II. 46,XX DSD:

Gonadal dysgenesis: In these patients, the development of the gonads and internal genitalia is abnormal. The external genitalia is often ambiguous and has been virilized depending on the function of the gonads.

- Pre-pubertal age (age 0-12): Hormonal evaluation: Low levels of inhibin and anti-müllerian hormone

- Pubertal and post-pubertal age (above 12 years old): Serum levels of luteinizing hormone and follicle stimulating hormone were elevated whereas testosterone, anti-müllerian hormone and Inhibin levels were low for age.

Androgen excess. This group comprises patients with congenital adrenal hyperplasia (CAH)[1]. In all included patients, a mutation of the gene of the CYP21 or 11B enzyme has been found. These patients presented with varying degree of virilization of the external genitalia whereas the internal genitalia were normally female. Serum levels of testosterone, 17-hydroxyprogesterone and or androstenedione are high.

Cloacal malformation: due to an anomalous development of the abdomen, the genital region remained severely underdeveloped. Gonads are normally developed and function well.

III. Sex Chromosome DSD: All patients with a sex chromosome abnormalities including Turner and Klinefelter mosaics.

1 This group also comprised three patients with virilization and normal female internal genitalia without high testosterone, 17-hydroxyprogesterone and or androstenedione but excluded in this study due to age below six years.

Exclusion criteria

Patients with all other types of DSD were excluded because these patients present different types of additional problems outside the focus or our study objectives:

- 46,XY DSD and syndromic associations of male genital development
- 46, XX DSD and syndromic associations
- Sex Chromosome DSD: Klinefelter and Turner syndromes without mosaicism

In addition, patients with limited intellectual capacities were excluded. The instruments applied in this study were designed for participants with intellectual abilities in the normal ranges. Judgments on intellectual functioning were based on interaction with the patients and (parental) reports on academic achievements. Due to the large variety of the development of gender identity and gender role behavior, the psychological assessment applied in gender development cannot assess well in children younger than 6 years old. Among other types of DSD, disorders in biosynthesis testosterone would follow the inclusion criteria but no patients entered the hospital.

Participation rate. Figure 2 displayed the patient selection for psychological study. From 286 patients diagnosed with DSD (Juniarto et al., 2013), 161 patients matched the inclusion criteria. Twenty-one patients were lost for follow-up, 29 patients declined participation due to unspecified reasons. Seven patients were diagnosed during the period of the study and were added to the research group. In total, 118 patients eventually joined the study.

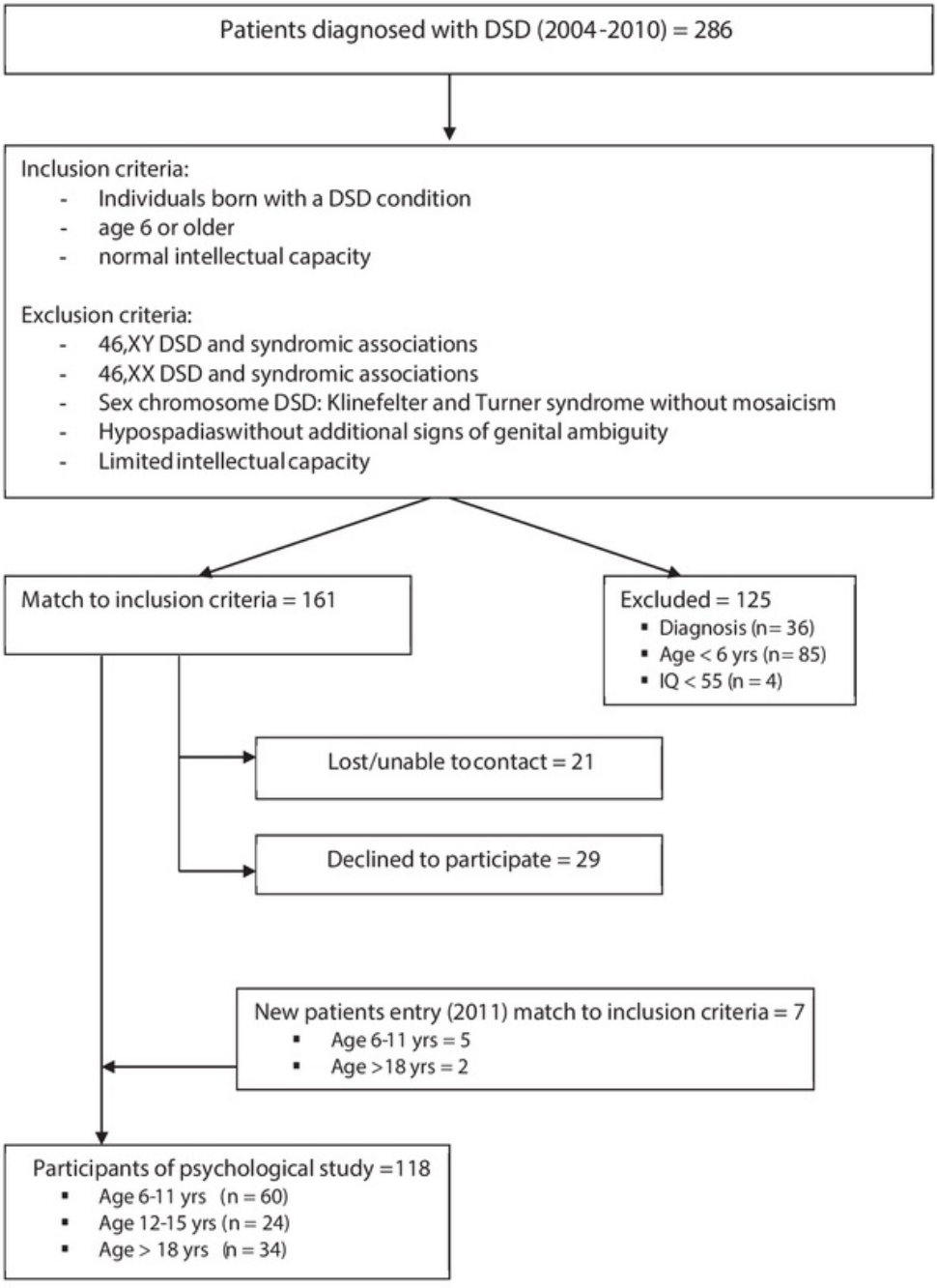

Figure 2. Patient selection for psychological study

Matched Control subjects

Initially, we planned to include non-affected siblings being raised in the same gender as the most appropriate control subjects because they share many social as well as biological characteristics, i.e. socioeconomic status, family characteristics to be raised in genetic similarities. Whenever it was impossible to choose a sibling (e.g. the patient has no same gender sibling), another family member or best friend was selected as control as long as the individual matched the inclusion criteria. While carrying out the study, difficulties in fulfilling the matching criteria became evident: Patients were the only child, the siblings were in the opposite gender, or no consent was given to involve sibling in the study because DSD was undisclosed in the family. Only three siblings joined the study. Therefore, the inclusion criteria for matched controls were expanded to include non-family-related individuals as control subjects. In order to serve as control the following criteria had to apply:

- Sibling or relative or best friend
- Healthy (having no DSD condition)
- In about similar age as patients (± 3 years)
- raised in the same gender
- Living in the same residential setting
- Voluntary participation in this study

Procedures

Data were collected between March 2007 until February 2011. The following procedures were applied in recruiting the participants and conducting the psychological assessment.

Patient recruitment. All patients in this study were under the care of the Sexual Adjustment Team (SAT) of Dr Kariadi Hospital and FMDU, Semarang, Indonesia. They were referred to SAT from in-patient or out-patient clinics (general practitioners, pediatricians, endocrinologists, gynecologists, urologists), and primary level of health providers. Other patients came by self-referral.

During the initial visit, the patients had a meeting with members of the SAT such as the clinical geneticist, pediatric endocrinologist, andrologist, and psychologist who are entitled to perform clinical, physical, and psychological examinations. These examinations were performed in the Dr. Kariadi Hospital. The medical diagnostic work up was performed by the geneticist in collaboration with the andrologist, endocrinologist, gynecologist, and other specialist member of the SAT. Information about the psychological study was given by the medical doctor, Achmad Zulfa Juniarto, to patients and/or parents. Subsequently, patients were invited to enroll into the medical and psychological study. After the parents and adult patients gave written consent to participate in the psychological study, the psychological assessment was conducted by a trained psychologist (AE), in the hospital or, if not feasible, at the patient's home.

Matched controls recruitment. Siblings were approached by parents or adult patients approval. Non-family matched controls were approached through local leaders (*Pak RT* or *Pak Lurah*) or midwives. In rural area, the *Pak Lurah* and midwife usually know very well the people who live in their neighborhood, so does the *Pak RT* in the urban areas. *Pak Lurah* and *Pak RT* are the leaders of the lowest level of government hierarchy. Study information was given by the researcher (AE). They were informed about this study comprised an evaluation on psychological well-being across children through adulthood initiated by the Psychology Faculty of the Diponegoro University in order to protect the patients from being identified by the matched controls subjects. Detailed information was described in chapter 4.

Psychological assessment. Subjects aged 6-17 years were interviewed separately from their parents. The original English versions of the questionnaires applied in this study were developed as paper-and-pencil measures. We came across about 15% of the patients and 20% of the parents who had received limited education or even were illiterate and many patients and parents had difficulties to fill out questionnaires due to unfamiliarity with self-reports (details on social demographic characteristics are described in chapter 3-7). In these patients and parents, we read the questions and response alternatives. The entire psychological interview took approximately 90 minutes for each patient. In case specialized help was needed for patients experiencing serious psychological problem, professional help was offered after assessment.

Instruments

See Table 1. The instruments are mainly quantitative measures, except the Social Stigmatization Scale for DSD (see Chapter 6) in which qualitative data were obtained to supplement the quantitative data. The Social Stigmatization scale for DSD is the instrument we developed for this study as no such scale was available.

Statistical Analysis

Various statistical methods have been applied in order to test for differences between patient and control groups. Detailed descriptions of applied statistical tests can be found in the chapters 3-7. Mainly quantitative methods were applied; however in the study on stigmatization (chapter 6), qualitative data were obtained as supplement to the quantitative data.

Methodological shortcomings

This study has several limitations. ***First***, concerning patient's participation. Twenty-one patients were lost to follow-up and 29 patients declined study participation. The reasons why patients moved out without notice or refused further contact with the DSD team remains unknown. One reason might be related to the geographical condition of the country. Indonesia is an archipelago, in which travelling between the island Java and other islands can be very costly. It is difficult to maintain contact and adhere to medical treatment when the patients move outside Java island. Besides the transportation and medical costs, patients often have to take day off from work which could reduce their income; these make the total costs of treatment very expensive for poor people. In view of the increasing number of newborns and toddlers suspected of DSD who were referred to our center, it is crucial to develop a structured program or treatment plan that provides the patient with life-long care.

Second, regarding sample representativeness. The majority of patients in this study came from poor families, living in the rural areas of the Central Java region, had received little to moderate education and earned a modest income. The same for the parents of children and adolescents. In order to be able to compare patient and control subjects on our psychological measures, we selected control subjects with a similar social background. We do not know to what extent findings of this study can be generalized to other patient groups in and outside Java, or to patients from other ethnicities. We have no

information regarding patients with DSD from higher socio-economic class or other ethnicities. We assume that more affluent Indonesian patients seek treatment in private clinics or visit hospitals abroad (i.e. in Singapore).

Third, we applied measures developed in Western society on non-Western participants. Several concepts we studied, i.e. concepts of femininity and masculinity are rooted in the culture. They may not have been culture-free. This raised the discussion if it was useful to translate questionnaires and semi-structured interviews and copy western methods of administration to a non-western country. From the study on psychometric properties we learned that most of the questionnaires had a scale structure in accordance with the original versions and that reliability was fair. However, methods to analyze psychometric properties of questionnaires demands participation of large groups of subjects. Methodologically it is best when this sample is representative for the entire population the measure is aimed for. Our sample contained students from different types of schools, colleges and universities in two provinces in the Central Java region. The students lived in sub-urban and urban areas. These areas have better infrastructures and living in these areas provides a larger access to all kind of social facilities such as schools, health care, better paid jobs etc. So our sample for the psychometric analysis was not fully representative for the entire Javanese population. As most of our patient and matched control groups lived in remote areas, here is a methodological shortcoming we could not overcome. Another methodologically shortcoming we could not solve is that we could apply paper and pencil or electronic versions of questionnaires to the reference groups, but had to administer questionnaires orally to our patient and matched control groups.

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Chapter 3

Body image and sexuality in Indonesian adults with disorders of sex development

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Abstract

In Indonesia, disorders of sex development (DSD) are not well-recognized and medical care for affected individuals is scarce. Consequently, many patients live with ambiguous genitalia and appearance. We compared reported outcomes on body image, sexual functioning, and sexual orientation of 39 adults with DSD (aged 18-41) and 39 healthy controls matched for gender, age, and residential status (urban, suburban, rural). Differences in gender and treatment status (treated or untreated) were also explored. On body image, adults with DSD reported dissatisfaction with sex-related body parts. Compared to the matched controls, women with DSD reported greater sexual distress; men with DSD reported lower erectile and ejaculation frequencies, more dissatisfaction with sexual life but not in sexual desire and activities. Men with DSD who had undergone genital surgery reported higher erectile and ejaculation frequencies than untreated men. More women than men in the DSD group reported a non-exclusive heterosexual orientation. DSD and infertility had a great impact on sexuality. Fear of ostracism complicated DSD acceptance. Findings were compared to those of Western studies. Based on these results, education about DSD and its psychosexual consequences may help to reduce the sexual distress and problems in adults with DSD and improve their quality of life.

Keywords: body image, sexual functioning, sexual orientation, disorders of sex development, Indonesia

Background

The management of disorders of sex development (DSD) in Indonesia faces significant barriers. In addition to the lack of diagnostic facilities, DSD conditions are also not well-recognized among the Indonesian population, including the majority of health care providers. Anomalies of the genital tract are often considered abnormal and shameful, leading to secrecy, social isolation, and stigmatization (Warne & Raza, 2008).

The most recently held consensus statements for clinical practices in DSD favor to prevent an ambiguous body appearance by giving hormonal treatment, removing gonads of individuals with 46,XY karyotype raised as females who were at risk for developing gonadal malignancies, and performing genital surgery (Joint LWPES/ESPE CAH working group, 2002; Hughes, Houk, Ahmed, Lee, & LWPES1/ESPE2 Consensus Group, 2006). Although still subject to debate (Köhler et al., 2012; Minto, Liao, Woodhouse, Ransley, & Creighton, 2003), these consensus statements also recommend early surgical correction of moderate to severely deviant genitalia. It is assumed that prevention of an ambiguous body and surgical correction will prevent social stigmatization and facilitate psychological adaptation to the assigned gender and sexual intercourse in adulthood (Carmichael & Alderson, 2004). Studies on psychosexual functioning have been initiated among patients with DSD who are living as either men or women. Impaired body image, problems in establishing romantic relationships, and difficulties with sexual functioning have been reported among patients with different diagnoses of DSD (Bouvattier, Mignot, Lefèvre, Morel, & Bougnères, 2006; Crouch, Liao, Woodhouse, Conway, & Creighton, 2008; Gastaud et al., 2007; Kojima et al., 2009; Migeon et al., 2002; Minto, Liao, Conway, & Creighton, 2003; Szarras-Czapnik, Lew-Starowicz, & Zucker, 2007; Wisniewski et al., 2000).

Before entrance, many Indonesian patients with DSD have never received medical assistance and consequently, they have been raised with ambiguous genitals and bodies for many years. In 1989, a multidisciplinary team was set up in collaboration between Dr. Kariadi Hospital and the Faculty of Medicine at Diponegoro University (FMDU), Semarang, Indonesia to provide diagnostic and medical care for these patients. The team was often confronted with psychosocial and psychosexual problems related to DSD. In collaboration with the Erasmus University Medical Center Rotterdam, a multidisciplinary study on the clinical diagnosis and treatment options for Indonesian patients with

DSD was initiated (Juniarto et al., 2012). As part of that study, we investigated body image and psychosexual functioning among Indonesian adults with DSD who became under medical attention late in life. Although genital ambiguity was often recognized at birth or body ambiguity developed in childhood or in adolescence, medical help-seeking was delayed for many years as patients, parents, and local health workers were ignorant about possibilities for medical help. So the majority of our patients never had received medical treatment for their DSD conditions before they entered our hospital in adolescence or adulthood. We therefore were able to study the course of development and its impact on the psychosexual and psychosocial aspects in whom medical treatment for the DSD were absent for most of their life.

Methods

Study design

The study was granted ethical approval by the board of the ethical commission at Faculty of Medicine, Diponegoro University (FMDU), Semarang Indonesia. This is a cross-sectional study comparing body image and psychosexual functioning between patients with DSD and their matched controls. All patients were managed clinically by the Sexual Adjustment Team of the Dr. Kariadi Hospital-FMDU.

Participants

The study sample was comprised of 39 patients, ages 18-41, diagnosed with DSD, who were living as man or woman (Table 1). Under Indonesian national law, legal gender assignment is obligatory and a third gender designation is impossible. All patients had normal intellectual functioning. Of 54 patients aged 18 or older who were diagnosed with DSD (Juniarto et al., 2012), five patients could not be contacted (due to invalid contact information) and ten patients refused to participate without giving explanation.

The matched control group consisted of 18 healthy women and 21 healthy men matched for age (with maximum age disparity of 3 years), gender, and residential settings (urban, suburban, or rural).

For the purpose of assessing psychometric properties of the measures that were utilized, a web-based survey has been set up to involve large group

of Indonesian adults. This web-based group comprised of 377 healthy adults who volunteered to respond this survey.

Instruments and Procedures

Translation and adaptation of the measures. In addition to qualitative data obtained from interviews, we evaluated the issues and concerns of participants in the areas of body image and psychosexual functioning with established measures. Since no validated Indonesian measures for psychosexual functioning were available, we therefore utilized Western measures that had been used in comparable studies on sexuality: Female Sexual Functioning Index (FSFI), Female Sexual Distress-Revised (FSDS-R), Body image scale (BIS), Male Sexual Health Questionnaire (MSHQ) (DeRogatis, Clayton, Lewis-D'Agostino, Wunderlich, & Fu, 2008; Lindgren & Pauly, 1975; Gastaud et al., 2007; Rosen et al., 2000; Rosen et al., 2004). Backward translation of these instruments into Indonesian language (Bahasa Indonesia) was conducted by a certified translator (UvA Talen). Prior to implementation, the researcher (AE) and a Dutch anthropologist specialized in research on sexuality in Indonesia and a good understanding of *Bahasa Indonesia* and English reviewed the Indonesian translations. The instruments' original scoring procedures were applied. All measures were piloted prior to the study. This pilot indicated that the questionnaires were best administered orally to clarify subjects' understanding of the questions prior to giving their response, particularly if subjects were unfamiliar with self-report questionnaires or had limited education

Table 1. Clinical characteristics and treatment history of patients with DSD

Subject	Karyotype	Diagnosis	Age (in year)		Type of treatments received
			at first visit*	at study visit	
Living as women (n=18)					
P01	46,XX	Congenital adrenal hyperplasia (CAH) [a]	11	19	Clitorodectomy at age 16 and HRT at age 16
P02	46,XX	Congenital adrenal hyperplasia (CAH) [a]	33	36	Clitoral reduction at age 34; HRT at age 36
P03	46,XX	Congenital adrenal hyperplasia (CAH) [a]	16	18	Clitoral reduction at age 7; HRT at age 8
P04	46,XY	Androgen Action Disorder (AAD) [b]	16	18	Gonadectomy at age 16; HRT at age 17
P05	46,XY	Androgen Action Disorder (AAD) [b]	12	18	None
P06	46,XY	Androgen Action Disorder (AAD) [b]	20	24	None
P07	46,XY	Androgen Action Disorder (AAD) [b]	19	19	None
P08	46,XY	Gonadal Dysgenesis (GD) [c]	13	18	Gonadectomy at age 10; HRT at age 14
P09	46,XY	Gonadal Dysgenesis (GD) [c]	39	39	None
P10	46,XY	Gonadal Dysgenesis (GD) [c]	27	27	None
P11	46,XY	Gonadal Dysgenesis (GD) [c]	23	23	None
P12	46,XY	Gonadal Dysgenesis (GD) [c]	19	19	None
P13	45,X (99%) / 46 XX,iXq	Gonadal Dysgenesis (GD) [c]	25	29	HRT at age 23; HRT (different types) at age 30
P14	46,XidicY	Gonadal Dysgenesis (GD) [c]	20	20	None
P15	46,Xi (X)(q10) (85%) / 45,X (15%)	Gonadal Dysgenesis (GD) [c]	20	20	None
P16	46,XY-(73%)/45,X(27%)	Gonadal Dysgenesis (GD) [c]	19	19	None
P17	46,X i(X)(q10) (24%) / 45,X (76%)	Gonadal Dysgenesis (GD) [c]	18	18	None
P18	46,XX	Other [d]	15	19	None

(continued)

Table 1. Clinical characteristics and treatment history of patients with DSD

(continued)

Subject	Karyotype	Diagnosis	Age (in year)		Type of treatments received
			at first visit*	at study visit	
Living as men (n=21)					
P19	46,XX	Congenital adrenal hyperplasia (CAH) [a]	17	22	None
P20	46,XX	Congenital adrenal hyperplasia (CAH) [a]	24	24	None
P21	46,XX	Gonadal Dysgenesis (GD) [c]	10	18	(received treatment at aged 7months and 7yr in other clinics; detailed information about the treatment was not available)
P22	46,XY	Androgen Action Disorder (AAD) [b] / PAIS	26	31	Gyneacomasty correction and chorda correction at age 24; hypospadia correction at age 26
P23	46,XY	Androgen Action Disorder (AAD) [b] / PAIS	16	20	Gyneacomasty reduction, chordectomy and hypospadia corrections at ages 14 and 15
P24	46,XY	Androgen Action Disorder (AAD) [b] / PAIS	12	18	Hypospadia correction at age 15
P25	46,XY	Androgen Action Disorder (AAD) [b]	23	26	Gynecomasty correction, chordectomy, hypospadia correction at age 23
P26	46,XY	Androgen Action Disorder (AAD) [b]	11	18	None
P27	46,XY	Androgen Action Disorder (AAD) [b]	27	27	None
P28	46,XY	Androgen Action Disorder (AAD) [b]	23	23	None
P29	46,XY	Gonadal Dysgenesis (GD) [c]	14	19	Gonadectomy at age 14
P30	46,XY	Gonadal Dysgenesis (GD) [c]	21	21	Chordectomy at age 11
P31	46,XY	Gonadal Dysgenesis (GD) [c]	14	21	None
P32	46,XY	Gonadal Dysgenesis (GD) [c]	41	41	None

(continued)

Table 1. *Clinical characteristics and treatment history of patients with DSD*

(continued)

Subject	Karyotype	Diagnosis	Age (in year)		Type of treatments received
			at first visit*	at study visit	
P33	46,XY	Gonadal Dysgenesis (GD) [c]	26	26	None
P34	46,XY	Unknown Under Masculinization [e]	14	19	Chordectomy at age 15; urethroplasty at age 19
P35	46,XY	Unknown Under Masculinization [e]	15	20	Hypospadia correction at age 5
P36	46,XY	Unknown Under Masculinization [e]	15	20	Penis bend (twice) and hypospadia corrections at ages 13, 15, and 16
P37	46,XY	Unknown Under Masculinization [e]	15	18	Chordectomy at age 15; urethroplasty at age 16
P38	46,XY	Unknown Under Masculinization [e]	29	29	Chordectomy at age 22 (in other clinic)
P39	46,XY	Unknown Under Masculinization [e]	17	20	None

Note. Men and women with DSD were assessed according to the gender they were living in at the time of study. HRT = hormone replacement therapy

* First time visit for medical treatment in our center (the Sexual Adjustment Team, FMDU/Dr. Kariadi Hospital).

[a] 46,XX CAH confirmed CYP 21 mutation in all patients.

[b] 46,XY DSD and under virilization. AR gene mutations had been confirmed in four men diagnosed with partial androgen insensitivity syndrome (PAIS) but not in the remaining patients. All subjects in this group had a normal hormonal testicular function with uni/bilaterally undescended testes. Androgen action is presumed not to be fully effective. Their clinical and biochemical presentation were close to those of subjects with a mutation in the androgen receptor with elevated serum levels of luteinizing hormone, testosterone, and anti-müllerian hormone, but the androgen receptor mutation could not be demonstrated.

[c] This group comprised of 10 patients with 46,XY karyotype (five men, five women), one men with 46,XX karyotype, and five women with sex chromosome abnormalities. All subjects had a normal hormonal testicular function with uni/bilaterally undescended testes. Androgen action is presumed to be fully effective. Their clinical and biochemical presentation is close to those of subjects with a mutation in the androgen receptor. Serum levels of luteinizing hormone and follicle stimulating hormone were elevated but levels of testosterone, anti-müllerian hormone, and Inhibin are low for age, and there was no diminished serum testosterone response to HCG.

[d] 46,XX DSD and cloacal malformation with genital ambiguity.

[e] 46,XY and under virilization. No cause for under masculinization could be identified. Serum hormone values and response to HCG were all normal for age.

Socio-demographic characteristics. Participants were asked about their age, gender, residential status, region of residence, religion, ethnicity, highest completed education level, marital status, and employment.

Body image. The Body Image Scale (BIS) measures the degree of (dis) satisfaction with body parts (Lindgren & Pauly, 1975). This scale consists of 30 items measuring the degree of (dis)satisfaction with different body parts, with a 5-point scale response options ranging from very satisfied (1) to very dissatisfied (5). The BIS originally consisted of three domains: primary sex characteristics, secondary sex characteristics, and so-called neutral body parts that are hormonally unresponsive e.g. eyes, hair (Lindgren & Pauly, 1975).

Female sexual distress. The Female Sexual Distress Scale-Revised (FSDS-R) measures frequency of sexual distress in women (DeRogatis et al., 2008). It consists of 13 items with a 5-point rating scale for response mode that varied from never (0), seldom (1), sometimes (2), often (3), and always (4). The Cronbach's alpha of the original FSDS-R is .86

Female sexual functioning. The Female Sexual Functioning Index (FSFI) measures sexual functioning in women who have been sexually active in the past four weeks (Rosen et al., 2000). It consists of 19 items with a 5-or-6 point response mode measuring different aspects of sexual functioning in sexually active women. Rosen et al (2000) reported that the FSFI consists of six domains of female sexual functioning: sexual desire, sexual arousal, lubrication, orgasm, satisfaction, and sexual pain. These domains demonstrated good internal reliability (Cronbach's alphas > .90 for all subscales) and good test-retest reliability (test-retest reliability scores ranged from .79 to .88). A section of the FSFI can be applied to women who have not been sexually active in the past four weeks; the number of items that can be applied is limited to sexual desire (item 1 and 2) and satisfaction of the overall sexual life (item 16) (Meyer-Bahlburg & Dolezal, 2007). The combined results of the FSFI and FSDS-R allow for the diagnosis of one or more sexual dysfunction(s) according to the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association. & American Psychiatric Association Task Force on DSM-IV, 2000). A FSFI score < 26.55 combined with a FSDS-R score > 11 implies the existence of at least one sexual dysfunction according to the DSM-IV-TR (Rosen et al., 2000).

Male sexual functioning. The Male Sexual Health Questionnaire (MSHQ) assesses male sexual functioning. It consists of 25 items with a 5 point response mode. The original English version of MSHQ has three domains of

sexual function: ejaculation, erection, and sexual satisfaction. A high degree of internal consistency and test-retest reliability of those domains were reported: Cronbach's alpha = .81, Pearson's r = .86 for erection; Cronbach's alpha = .90, Pearson's r = .87 for ejaculation; Cronbach's alpha = .90, Pearson's r = .88 for sexual satisfaction (Rosen et al., 2004).

Sexual orientation. The Kinsey Rating Scale on adult sexual orientation measures sexual orientation using a 7-point rating scale ranging from exclusively homosexual to exclusively heterosexual (Kinsey, Pomeroy, & Martin, 1948, 1953) in sexual attraction, sexual relationships, romantic fantasy, erotic fantasy, and self-identification. To enable a proper statistical analysis, one option of response ('no experience') was added. Subsequently, the subjects' responses were recoded into four categories: exclusively homosexual (1), exclusively heterosexual (2), nonexclusive orientation (3), and no experience (4) (Zucker et al., 1996). We presented subjects' response on each item. The concepts of heterosexuality and homosexuality were used in this study in accordance with the presented gender, not the chromosomal sex. In Indonesia, the term "homosexuality" is unfamiliar and often misunderstood or perceived negatively by the general population. Therefore, we applied the terms of 'man-to-man' or 'woman-to-woman' or 'same sex' to refer to homosexuality or homosexual. The interviewer began assessing subjects' experiences on their first love, dating, and sexual activities with the opposite gender, then probing to possibility of having similar experiences (imagery or behavior) with person of the same sex.

Procedures. Data were collected between March 2007 and May 2011. Following diagnostic procedures confirming the diagnosis of DSD (Juniarto et al., 2012), patients were invited to participate. Verbal and written study information was provided by a physician (AZJ). After the patient agreed to participate and had given written consent, an appointment for a psychological assessment was made. This assessment was performed at the hospital in all cases, except one in which the patient asked to have the assessment at home. The psychological assessment was conducted by a clinical psychologist (AE) who had been trained to deliver the applied measures and to conduct interviews with patients with DSD. A small gift or reimbursement of transportation and a meal were provided for their participation. Men and women with DSD were interviewed according to the gender they lived in at the time of study.

Initially, the study design aimed to include siblings as matched controls

but this was unfeasible in terms of the demographic matching and secrecy of the DSD condition within the family. The researcher (AE) subsequently recruited healthy participants who matched those with DSD in terms of residential status, gender, age (matching factors). The researcher informed the matched control subjects about the study but only said that they were asked to participate in a study on psychosexual development in adults carried out by the Psychology Faculty of the Diponegoro University in Semarang, in order to protect the patients from being identified as patients with DSD by their matched controls. After they received study information, the healthy control subjects were invited to join the study. After giving written consent, matched control subjects followed procedures similar to the patient group. A small gift was provided for their participation. All matched control subjects requested that the assessments to be conducted at home.

Regarding the web-based survey that was setup to assess psychometric properties of the instruments that were utilized, we sent an email invitation to several mailing lists for Indonesian adults. The recipient was encouraged to forward the email invitation to other adults in their contacts. The study aim, principal investigator and affiliation, time estimated for completion of the measures and confidentiality assurance were provided on the welcome page prior to participation. The survey was conducted within a period of four weeks. Socio-demographic data, such as occupation and educational level, showed that the web-based control group differed substantially from the patient and matched control groups with respect to socioeconomic status and education; the web-based control subjects came from well to do families (university graduates and have well-paid jobs) whereas most patient and matched control subjects came from poor families. This socio-demographic differences affected results. Data from the web-based controls were not presented for the targeted comparisons but were used to validate the measures only.

Statistical analysis

Construct validity was explored using principal component analysis (PCA) with varimax rotation and Kaizer normalization. Instrument reliability was evaluated as internal consistency with Cronbach's Alpha as the outcome measure. We report the optimal model for the Indonesian data, even when that model deviates from the original Western model. Only responses without missing data were used in the statistical analyses. Differences in continuous data

between groups were compared using the Mann-Whitney *U* test. Differences in categorical data were compared using the Fisher's Exact test. Differences were considered significant at $p < .05$ (two-sided). Because of the small number of patients (Table 1), comparison among diagnostic subgroups was impossible.

Results

Participants

Table 2 shows participant's socio-demographic characteristics. The matched control and patient groups were not significantly different, except in marital status. There were no significant differences between treated and untreated patients. However, untreated patients tended to be older than treated patients when they first visited our hospital.

Table 2. *Sociodemographic characteristics of study participants*

Sociodemographic characteristics	Adults with DSD (*n*=39)	Matched Controls (*n*=39)	*p*[a]	Treated patients (*n*=18)	Untreated patients (*n*=21)	*p*[b]
Age of visit (in year)	*M* ± SD	*M* ± SD		*M* ± SD	*M* ± SD	
at first admission	19.9 ± 7.3	-	.09	18.0 ± 6.6	21.5 ± 7.6	.09
at study visit	22.6 ± 5.9	23.3 ± 4.7		22.0 ± 5.5	23.1 ± 6.3	.31
	n (%)	*n* (%)		*n* (%)	*n* (%)	
Gender						
Male	21 (53.8)	21 (53.8)	.99	12 (66.7)	9 (42.9)	.20
Female	18 (46.2)	18 (46.2)		6 (33.3)	12 (57.1)	
Residential settings						
Rural	18 (46.2)	18 (46.2)	.99	7 (38.9)	11 (52.4)	.54
Suburban	13 (33.3)	13 (33.3)		6 (33.3)	7 (33.3)	
Urban	8 (20.5)	8 (20.5)		5 (27.8)	3 (14.3)	
Residence/province						
Central Java	32 (82.1)	37 (94.9)	.23	14 (77.8)	18 (85.7)	.47
Other provinces in Java	4 (10.3)	1 (2.6)		3 (16.7)	1 (4.8)	
Outside Java island	3 (7.7)	1 (2.6)		1 (5.6)	2 (9.5)	
Ethnicity						
Javanese	35 (89.7)	38 (97.4)	.36	15 (83.3)	20 (95.2)	.32
Non Javanese	4 (10.3)	1 (2.6)		3 (16.7)	1 (4.8)	
Religion						
Islam	38 (97.4)	32 (82.1)	.05	18 (100.0)	20 (95.2)	.99
Other	1 (2.6)	7 (17.9)		0	1 (4.8)	
Marital status						
Men						
Married	3 (14.3)	21 (100)	<.001	2 (16.7)	1 (11.1)	.99
Never married	18 (85.7)	0		10 (83.3)	8 (88.9)	
Women						
Married	1 (5.6)	18 (100)	<.001	1 (16.7)	0	.33
Never married	17 (94.4)	0		5 (83.3)	12 (100)	
Highest Educational level*						
Men						
Illiterate	2 (9.5)	1 (4.8)	.55	0	2 (22.2)	.08
Elementary school	2 (9.5)	2 (9.5)		2 (16.7)	0	
High school	16 (76.2)	14 (66.7)		10 (83.3)	6 (66.7)	
Higher education	1 (4.8)	4 (19.0)		0	1 (11.1)	
Women						
Illiterate	2 (11.1)	0	.52	1 (16.7)	1 (8.3)	.71
Elementary school	1 (5.6)	0		0	1 (8.3)	
High school	12 (66.7)	14 (77.8)		5 (83.3)	7 (58.3)	
Higher education	3 (16.7)	4 (22.2)		0	3 (25.0)	
Occupation						
Men						
Unemployed	8 (38.1)	1 (4.8)	.06	5 (41.7)	3 (33.3)	.92
Labor	7 (33.3)	9 (42.9)		3 (25.0)	4 (44.4)	
Self-employed	3 (14.3)	4 (19.0)		2 (16.7)	1 (11.1)	
Staff	3 (14.3)	7 (33.3)		2 (16.7)	1 (11.1)	
Women						
Unemployed	5 (27.8)	10 (55.6)	.14	3 (50.0)	7 (58.3)	.54
Labor	1 (5.6)	1 (5.6)		1 (16.7)	0	
Self-employed	4 (22.2)	0		0	0	
Staff	8 (44.4)	7 (38.9)		2 (33.3)	5 (41.7)	

[a] Patients and the matched controls comparison. [b] Treated and untreated patients's comparison.

Reliability and validity of the measures

As mentioned in the method section, the validity and reliability of measures applied in this study were obtained using data of the web controls. The results of reliability and validity analyses are presented in Table 3.

The Indonesian versions of the instruments had good psychometric properties and the components generated from these analyses were relevant to the constructs assessed in the original measures. The BIS comprises one component similar to the original version; the FSDS-R comprises one component similar to the original model but also facilitates a 2-component model to assess cognitive and affective components of sexual distress. In the FSFI, items measuring frequency and difficulties in lubrication and orgasm are loaded separately. Similarly, in the MSHQ, items measuring frequency and difficulties in erection and ejaculation functioning are loaded separately. A few minor differences with the original versions are addressed in Table 3.

Body image

In general view on the body (Table 4a), men with DSD did not differ significantly from the matched control men whereas in women, there was a tendency towards significance that women with DSD reported greater dissatisfaction with their body than the matched control women.

Table 4a. Body Image Scale: Global score of body image across groups

Subjects	Adults with DSD	Matched controls	p^a	Treated patients	Untreated patients	p^b
Women	$n = 18$ 3 (2-3)	$n = 18$ 2 (1-3)	.06	$n = 6$ 2.5 (2-3)	$n = 12$ 3 (2-3)	.99
Men	$n = 21$ 2 (1-3)	$n = 21$ 3 (1-3)	.59	$n = 12$ 3 (1-3)	$n = 9$ 2 (1-3)	.29

Note. Data were presented in median and range. A higher value indicates greater dissatisfaction with the body parts. The Mann-Whitney U-test was applied. Men and women with DSD were assessed according to the gender they were living in at the time of study. Adopted from the Body Image Scale (BIS) from Lindgren, T. W., & Pauly, I. B. (1975). A body image scale for evaluating transsexuals. *Archives of Sexual Behavior, 4*(6), 639-656. doi:10.1007/bf01544272. A five-point response mode was applied: very satisfied (1), satisfied (2), neutral (3), dissatisfied (4), and very dissatisfied (5).

[a] Comparison between the patients and the matched control groups

[b] Comparison between treated and untreated group of patients.

Table 3. Results of principal component analysis (PCA) and reliability analysis

Measures	N	N of components (% of total variance explained)	Components and item distributions	Cronbach's alpha (α)
Body Image Scale (BIS) Woman version [a]	161	1 PC (53.4)	General body image (all items) Sex-related body parts: items 6,9,14,22,24	.97 .86
Man version [a]	82	1 PC (66.7)	General body image (all items) Sex-related body parts: items 6,9,14,18,22,27	.98 .93
Female Sexual Distress Scale-Revised / FSDS-R [b]	185	2 PC (55.1)	Affective sexual distress (items 1,2,3,4,5,11,12) Cognitive sexual distress (items 6,7,8,9,10,13) Overall sexual distress (all items)	.91 .85 .93
Female Sexual Functioning Index / FSFI [c]	94	6 PC (66.7)	Sexual desire (items 1,2) Arousal/lubrication frequency (items 3,4,5,6,7,9) Difficulty in lubrication & orgasm (items 8,10,12) Orgasm frequency & pleasure (items 11,13) Satisfaction with sexual life (items 14,15,16) Pain (items 17,18,19)	.79 .81 .90 .69 .91 .89
Male Sexual Health Questionnaire / MSHQ [d]	41	4 PC (53.8)	Erection & ejaculation frequency (items 1,2,3,5,6,7,11,21) Erection & ejaculation dysfunction (items 4, 8,9,10,12,20,24) Satisfaction with sexual life (items 13-18) Sexual desire & activity (19,22,23,25)	.77 .58 .89 .61
Kinsey Rating Scale of Adult Sexual Orientation [e]	210 (142 women; 68 men)	1 PC (96.6)	All items	.99

Note. [a] BIS was originally developed for assessing body image in transgender persons. Three domains of sexual characteristics were measured in the original scale: primary, secondary, and neutral (hormonally unresponsive). The test-retest reliability of the original BIS showed good consistency (Lindgren & Pauly, 1975). Our findings correspond to one component of general body image. As DSD conditions might impact in body image, in this study we included primary sexual characteristics for further comparison analysis after evaluated the internal consistency.

[b] Originally FSDS-R consists of one component measuring overall sexual distress using total score. The Cronbach's alpha of the original scale is .86 (DeRogatis et al., 2008). Our findings demonstrated two components of sexual distress: cognitive and affective components of sexual distress. In this study, we included overall sexual distress for further comparison analysis after evaluating the internal consistency.

[c] The Cronbach's alphas of the original FSFI scales are: Desire scale: α = .92; Arousal scale: .95; Lubrication

scale: α = .96; Orgasm scale: α = .96; sexual satisfaction scale: α = .89; Pain scale: α = .94 (Rosen et al., 2000). In our study, items measuring frequency and difficulties in lubrication and orgasm were loading into two different components. Due to lack of sexual activity and absence of a partner during the past four weeks, we applied items of sexual desire (items 1 and 2) and of satisfaction with overall sexual life (items 16) for further analysis.

[d] The Cronbach's alphas of the original MSHQ scales are: erection scale: α = .81; ejaculation scale: α = .90; sexual satisfaction scale: α = .90 (Rosen et al., 2004). In our study, items measuring frequency and difficulties in erection and ejaculation functioning were loading into two different components.

[e] Statistical analysis using sum score was inapplicable because the majority of patients reported lack of sexual experiences. Subsequently, comparison analysis was performed on each item.

However, as demonstrated in Table 4b, patients with DSD generally experienced greater dissatisfaction with their genitalia and other sex- related body parts than controls. Significant differences were reported, particularly on ovaries/uterus, breasts, vagina (in women); penis, scrotum, testes (in men). There were no differences between treated and untreated men and women (Tables 4a and 4b). Almost all patients had ambiguous genitalia, and ambiguous sex-related body parts such as underdeveloped breasts, low-pitched voice in women, and sparse facial hair in men.

Table 4b. Body Image Scale: dissatisfaction and satisfaction with sex-related body parts

Sex-related body parts	Dissatisfaction		Satisfaction		*p*
	Adults with DSD	Match controls	Adults with DSD	Match controls	
Women	*n* = 18	*n* = 18	*n* = 18	*n* = 18	
Ovaries/uterus	7 (38.9)	0	4 (22.2)	16 (88.9)	<.001
Breasts	6 (33.4)	0	6 (33.3)	14 (77.8)	.02
Voice	4 (22.3)	0	9 (50.0)	13 (72.2)	.37
Vagina	4 (22.2)	0	7 (38.9)	15 (83.4)	.05
Clitoris	2 (11.1)	0	7 (38.9)	13 (72.2)	.11
Men	*n* = 21	*n* = 21	*n* = 21	*n* = 21	
Penis	17 (81.0)	0	1 (4.8)	14 (66.7)	<.001
Scrotum	12 (57.2)	0	6 (28.6)	10 (47.6)	<.001
Testes	10 (47.6)	0	5 (23.8)	10 (47.6)	.004
Facial hair	4 (19.0)	2 (9.5)	8 (38.1)	6 (28.6)	.62
Body hair	3 (14.3)	1 (4.8)	10 (47.6)	8 (28.1)	.40
Breasts	4 (19.1)	0	10 (47.6)	10 (47.6)	.30

Notes. Data were presented as *n* (%). Dissatisfaction responses comprised "dissatisfied" and "very dissatisfied" responses on the Body Image Scale (BIS) whereas satisfaction responses comprised "satisfied" and "very satisfied" responses on BIS. The Fisher's Exact test was applied.

Sexual functioning

Table 5 summarizes the findings on sexual functioning across groups.

Female sexual functioning (FSFI). In line with marital status (Table 2), only one woman with a DSD reported she had been sexually active in the

last four weeks whereas all matched control women reported they had been sexually active during that period. Women with DSD reported no differences from the matched control women in terms of sexual desire. They reported less satisfaction with their overall sexual life than control women. In response to the item measuring satisfaction with the overall sexual life, only two (11.1%) women with DSD reported satisfaction with their sexual life compared to 88.9% of matched-control women. Treated and untreated women with DSD did not differ in sexual desire or satisfaction with sexual life.

Female sexual distress (FSDS-R). Women with DSD reported greater affective and cognitive sexual distress than the matched control women; 72% of women with DSD reported a sexual distress (score above the cut-off point of 11), whereas among matched control women this percentages was 11% ($p < .001$). No differences in sexual distress were found between treated and untreated women with DSD although the median values of FSDS-R are above the cut-off score (Table 5).

Male sexual functioning (MSHQ). Men with DSD reported lower frequencies of erections and ejaculations or less satisfaction with sexual life than control men, but they did not report better functioning in erections and ejaculations or lower sexual desire or less sexual activities (Table 5). Men with DSD who had received treatment reported higher frequencies of erections and ejaculations than untreated men with DSD; however, they did not report better functioning in erections and ejaculations, or greater satisfaction with sexual life, or higher sexual desire or more sexual activities than untreated men with DSD. Two out of four married men with DSD reported an inability to penetrate. This made them feel less capable of satisfying their wives.

Table 5. Sexual functioning across groups (data on FSFI, FSDS-R, and MSHQ)

Measures	Adults with DSD	Matched controls	p^e	Treated patients	Untreated patients	p^f
	Mdn (min-max)	*Mdn* (min-max)		*Mdn* (min-max)	*Mdn* (min-max)	
FSFI[a]	*n* = 18	*n* = 18		*n* = 6	*n* = 12	
Sexual Desire (sum of items 1 & 2)	4 (2-8)	5.5 (3-8)	.13	4 (2-8)	4 (2-8)	.79
Satisfaction with sexual life (item 16)	0 (0-5)	5 (2-5)	**<.001**	0 (0-5)	0 (0-0)	.09
FSDS-R[b]						
Overall sexual distress	19.5 (0-49)	2 (0-21)	**<.001**	15.5 (0-30)	20 (0-49)	.42
Affective sexual distress[c]	12.9 (0-30.4)	0 (0-15.2)	**<.001**	10.5 (0-15.2)	12.9 (0-30.4)	.39
Cognitive sexual distress	8 (0-24)	1 (0-8)	**<.001**	9 (0-17)	8 (0-24)	.73
MSHQ[d]	*n* = 21	*n* = 21		*n* = 12	*n* = 9	
Erection and ejaculation frequency[a]	32 (13-40)	37 (26-40)	**.03**	36.5 (18-40)	31 (13-38)	.05
Erection and ejaculation dysfunction[d]	27 (15-31)	29 (24-31)	.33	27 (15-31)	27 (15-31)	.51
Satisfaction with sexual life[a]	18 (13-27)	24 (17-30)	**<.001**	18 (13-27)	18 (14-24)	.85
Sexual desire and activity[a]	11 (9-20)	13 (8-17)	.54	11 (9-15)	12 (9-20)	.92

Note. Men and women with DSD were assessed according to the gender they were living in at the time of study. FSFI = Female Sexual Functioning Index; FSDS-R = Female Sexual Distress Scale-Revised; MSHQ = Male Sexual Health Questionnaire.

[a] It consists of 19 items with five or six point response mode. Score range: 0-5 or 1-5. A higher value indicates better sexual functioning.

[b] It consists of 13 items with a five point response mode: never (0), seldom (1), sometimes (2), often (3), and always (4). A higher value indicates greater sexual distress.

[c] Sum scores multiplied by 1.17 for equal comparison to cognitive-related distress.

[d] It consists of 25 items with a five and six point response mode. Score range: 0-5 or 1-5. A higher value indicates better sexual functioning, except in the Erection and ejaculation dysfunction that a higher value indicates a higher degree of (sexual) dysfunction.

[e] Comparison between the study group and the matched control group.

[f] Comparison between the treated and the untreated groups of patients with DSD.

Sexual relationships. Sixteen women and 20 men with DSD reported they had been "in love". For this subgroup, 14 women (77.7%) and seven men (35%) had never had romantic relationships (Table 6). During the interviews with patients, it appeared that fear of rejection by a partner due to infertility was the major reason they did not pursue romantic relationships. Women with DSD also appeared to be emotionally sensitive and preferred to delay or refuse to engage in a romantic relationship to avoid partner's rejection. One woman and three men with DSD had preferred to end their dating relationships without disclosing their infertility. Three married men with DSD noted the importance of family support in helping them live with DSD and disclose infertility to their spouses. Interestingly, their spouses verbalized acceptance of their DSD condition. Another man with DSD changed his stated intention to marry a single woman and instead, married a widow with children from her previous marriage. This helped him to reduce his anxiety that he would not be able to satisfy his spouse because of his inability to penetrate and to make her pregnant. A married woman with DSD, who received emotional support from parents and siblings, finally disclosed her infertility to her husband. The result was divorce, after she declined his request for polygamy.

Sexual orientation

Table 6 shows that more patients than controls had no sexual experiences. Nine patients (23.1%) reported they had never had romantic/erotic fantasies and 21 patients (53.8%) never engaged in sexual relations because they considered it sinful or taboo. Generally, more women with DSD reported non-exclusive or exclusive homosexual orientation than matched control women with respect to falling in love and sexual relationships. In contrast, men with DSD were similar to the matched control men with respect to their sexual orientation, favoring an exclusively heterosexual focus.

Table 6. Response distribution on the Kinsey Rating Scale of sexual orientation

Items and response categories	Adults with DSD	Matched controls	p^a	Treated patients	Untreated patients	p^b
Living as women	*n = 18*	*n = 18*		*n = 6*	*n = 12*	
1. Falling in love	*n* (%)	*n* (%)		*n* (%)	*n* (%)	
Exclusively homosexual	2 (11.1)	0	.04	0	2 (16.7)	.85
Exclusively heterosexual	13 (72.2)	18 (100.0)		5 (83.3)	8 (66.7)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	2 (11.1)	0		1 (16.7)	1 (8.3)	
2. Sexual relationships						
Exclusively homosexual	1 (5.6)	0	<.001	0	1 (8.3)	.99
Exclusively heterosexual	3 (16.7)	15 (83.3)		1 (16.7)	2 (16.7)	
Non-exclusive orientation	0	0		0	0	
No experience	14 (77.8)	3 (16.7)		5 (83.3)	9 (75.0)	
3. Romantic fantasy						
Exclusively homosexual	2 (11.1)	0	.17	0	2 (16.7)	.64
Exclusively heterosexual	11 (61.1)	16 (88.9)		5 (83.3)	6 (50.0)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	4 (22.2)	2 (11.1)		1 (16.7)	3 (25.0)	
4. Erotic fantasy						
Exclusively homosexual	2 (11.1)	0	.11	0	2 (16.70	.87
Exclusively heterosexual	10 (55.6)	16 (88.9)		4 (66.7)	6 (50.0)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	5 (27.8)	2 (11.1)		2 (33.3)	3 (25.0)	
5. Self-identification						
Exclusively homosexual	0	0	.49	0	0	.99
Exclusively heterosexual	16 (88.9)	18 (100.0)		6 (100)	10 (83.3)	
Non-exclusive orientation	1 (5.6)	0		0	1 (8.3)	
No experience	1 (5.6)	0		0	1 (8.3)	
Living as men	*n = 21*	*n = 21*		*n=12*	*n=9*	
1. Falling in love						
Exclusively homosexual	0	0	.11	0	0	.99
Exclusively heterosexual	20 (95.2)	17 (81.0)		11 (91.7)	9 (100.0)	
Non-exclusive orientation	0	4 (19.0)		0	0	
No experience	1 (4.8)	0		1 (8.3)	0	
2. Sexual relationships						
Exclusively homosexual	0	0	.28	0	0	.99
Exclusively heterosexual	14 (66.7)	17 (81.0)		8 (66.7)	6 (66.7)	
Non-exclusive orientation	0	1 (4.8)		0	0	
No experience	7 (33.3)	3 (14.3)		4 (33.3)	3 (33.3)	
3. Romantic fantasy						
Exclusively homosexual	0	0	.23	0	0	.99
Exclusively heterosexual	21 (100.0)	18 (85.7)		12 (100.0)	9 (100.0)	
Non-exclusive orientation	0	1 (4.8)		0	0	
No experience	0	2 (9.5)		0	0	

(continued)

Table 6. Response distribution on the Kinsey Rating Scale of sexual orientation

(continued)

Items and response categories	Adults with DSD	Matched controls	p^a	Treated patients	Untreated patients	p^b
Living as men	*n = 21*	*n = 21*		*n=12*	*n=9*	
4. Erotic fantasy						
Exclusively homosexual	0	0	.99	0	0	.99
Exclusively heterosexual	20 (95.2)	20 (95.2)		11 (91.7)	9 (100.0)	
Non-exclusive orientation	0	0		0	0	
No experience	1 (4.8)	1 (4.8)		1 (8.3)	0	
5. Self-identification						
Exclusively homosexual	0	0	.99	0	0	.17
Exclusively heterosexual	19 (90.5)	20 (95.2)		12 (100.0)	7 (77.8)	
Non-exclusive orientation	2 (9.5)	1 (4.8)		0	2 (22.2)	
No experience	0	0		0	0	

Note. Men and women with DSD were assessed according to the gender they were living in at the time of study. Initially, a seven-point scale of response mode was applied, range from exclusively homosexual to exclusively heterosexual. However, sum scores could not be obtained due to participant's lack of sexual experiences. To enable a proper statistical analysis, the participant responses were categorized into four groups: exclusively homosexual, exclusively heterosexual, non-exclusive orientation, and no experience.

[a] Comparison between the patient and the matched control groups.

[b] Comparison between the treated and the untreated groups of patients with DSD. The Fisher's Exact test was applied.

All four patients with 46,XX karyotype and CAH reported exclusively heterosexual orientations: two patients with 46,XX karyotype and CAH, living as men reported they only felt sexually attracted to women whereas two patients with 46,XX karyotype and CAH living as women reported they only felt sexually attracted to men. Non-exclusive heterosexual orientation was reported by six out of 14 untreated patients with the 46,XY karyotype, living as men or women. Among these patients, one man with an androgen action disorder and one man with gonadal dysgenesis identified themselves as non-exclusive heterosexual focus, but did not report any non-exclusive heterosexual fantasies or behaviors. Both men concluded that their sexual identification could not be exclusively heterosexual because of their DSD condition. Four out of nine women with 46,XY karyotype (two women with androgen action disorder, two women with gonadal dysgenesis) reported varying degrees of non-exclusively heterosexual fantasies or behaviors, but identified themselves as exclusively heterosexual.

Discussion

We studied psychosexual functioning among Indonesian adults with DSD who had been identified and treated late in life. These patients had been raised with and continued to live with ambiguous bodies and encountered barriers to seek a spouse and marry; in Indonesia a major step forward into being respected as an adult and acquire full independency, particularly for women. Concerns about these psychosocial issues of gender and sexuality presented to the health care professionals on the Sexual Adjustment Team at the Dr Kariadi Hospital/Faculty of Medicine, Diponegoro University gave rise to the study. Our major aim was to quantify these psychosexual problems in patients with DSD and compare them to healthy subjects. To our knowledge, this is the first such study performed in Indonesia.

Body image, sexual distress, and sexual functioning

Results on body image revealed that patients with DSD, untreated or treated late in life, were dissatisfied with their sex-related body parts, but not with their bodies in general. These results suggest that body ambiguity causes considerable distress in adults affected with DSD. Early diagnosis and treatment may decrease body ambiguity during puberty and hence, prevent these psychosocial consequences and may improve quality of life. As stated in the Consensus statement (Hughes et al., 2006), treatment of DSD comprises the entire diagnostic process, education on parents about diagnosis and treatment possibilities, surgically and hormonally, and facilitating parents and/or adult patients to make decisions with respect to treatment/no treatment they consider will be best for their child. Educating health care practitioners and raising public awareness of DSD as a medical condition are essential for improving the social functioning and quality of life of patients with DSD.

Most women with DSD had never been involved in romantic relationships. They also reported greater sexual distress, less sexual experiences, and felt less satisfied with their sexual life than control women. Low libido and lack of initiatives to seek a partner despite social expectancy to do so, and fear of social consequences due to infertility probably lowered their satisfaction with sexual life. The qualitative interviews indicated that body ambiguity induced negative thoughts and feelings about themselves in women with DSD. Studies in Western women with DSD also observed problems in sexual

desire, sexual arousal, and entering partner relationships (Gastaud et al., 2008; Köhler et al., 2012).

Treated and untreated women with DSD reported sexual distress. The interview data suggested that their DSD conditions and related infertility were related to this sexual distress. Fear of disclosure and possible negative consequences of disclosure on their social position (divorce or polygamy) prevented these women from entering romantic relationships. One significant consequence of this was a failure to meet the social expectation of marriage, which caused substantial distress. Western studies on psychosexual functioning in women with DSD have also reported low desire and lack of sexual experiences among other problems in sexual functioning (Gastaud et al., 2007; Minto et al., 2003; Szarras-Czapnik et al., 2007). These women also felt reluctant to enter sexual relationships because of the need for disclosure of their DSD condition and uncertainty about the partner response—which could include outright rejection. In contrast, Western societies are less collectively driven than the Indonesian society is, and thus, there is less pressure to marry and have children.

Previous studies reported increased erectile functioning and ejaculations among men with DSD who had received treatment i.e. hypospadia corrections (Bouvattier et al., 2006; Kojima et al., 2009; Migeon et al., 2002). In our study, men with DSD who had received hypospadia corrections reported better erectile functioning and more ejaculations than untreated men. As we had no data on genital and sexual functioning before surgery, we had to rely on patients' self-reports. In comparison to their matched controls, men with DSD reported lower frequencies of erection and ejaculation but this did not influence their sexual desire and activities.

Sexual relationships

In Indonesia, intimate relationships are only legalized within marriage; premarital sex is socially unacceptable and regarded as sinful from a religious perspective. Although, premarital sex does occur as suggested from our web-based study, very limited or no sexual experience was reported by patients with DSD. These findings differ from prior studies reporting marital and premarital sexual experiences in men and women with DSD (Gastaud et al., 2007; Kojima et al., 2009), indicating that culture plays a significant role in sexual behavior in individuals with DSD.

Our study group included more men than women in established, romantic relationships. There are two explanations for this. First, men and women may use different strategies to cope with DSD. Women with DSD appear to be more emotionally sensitive and tended to avoid the risks of social rejection by delaying or not engaging in romantic relationships. Men with DSD also experienced distress but were more willing to enter into these types of relationships. Second, women are more subject to blame in terms of infertility rather than men. Pregnancy undoubtedly indicates female fertility; however, the absence of pregnancy was more often regarded as the impact of female infertility rather than male infertility. As procreation is a major reason for marriage among Indonesians, in the case of infertility, particularly among Moslem, men has more options than women: to divorce and marry another woman, or go for polygamy. No one will blame the infertile man because he obeys the social demand to procreate and he is allowed to do so by his religious values. He might receive sympathy for being unfortunate not to have children after several marriages. His infertility remains undisclosed unless he intends to reveal it through fertility tests. Infertility due to DSD makes life much harder for adults. The fear of rejection led to unwillingness to disclose DSD and related infertility, even within the family. As a consequence, patients dealt with their sadness alone and their lack of initiatives to seek a partner was often not understood, even by their own relatives who pressured them to get married and have children. Facilitating disclosure, family support, and more realistic expectations may reduce this sense of isolation, psychological distress, and level of acceptance for both patient and family. Four men in this study reported this type of family support, however, few women in the study experienced this and one woman was faced with divorce when she disclosed her DSD. This may explain why men with DSD in this study were more willing to take initiatives to seek romantic partners than did the women with DSD.

Sexual orientation

Two out of 20 men with DSD identified themselves as non-exclusively heterosexual. They thought having a DSD was abnormal, and therefore, their sexual orientation should not be similar to people without a DSD. Non-exclusive heterosexual orientation was higher among women with DSD than among the matched controls. Similar findings have been reported in Western studies of women with 46,XX karyotype and CAH and patients with 46, XY karyotype and partial action of and sensitivity for androgens, stressing the importance of prenatal action of androgens (Köhler et al., 2012; Meyer-Bahlburg, Dolezal, Baker, & New, 2008; Nordenstrom et al., 2010). Women with DSD who reported various degrees of non-exclusively heterosexual orientation in fantasy or behavior did not identify themselves as non-exclusive heterosexually-oriented possibly to conform to socially acceptable norms and attitudes. This indicates that social influences are important in reporting sexual orientation among patients with DSD living in a collectively-driven society. Unfortunately, lack of published data disallows any comparison of our findings on sexual orientation to similar studies in Asian patients with DSD or data on homosexuality or bisexuality among the Indonesian population.

Treated and untreated groups comparison

Comparison between treated and untreated groups of patients did not reveal any differences in reported (dis)satisfaction with their body parts, sexual distress, and main aspects of sexual functioning.

Despite early detection of the ambiguous genital, for all patients (except five patients) medical help was delayed for many years as patients, parents and medical helpers were not aware that medical treatment was available, Both treated and untreated groups of patients entered our medical service in adolescence or adulthood. Prior to entering our medical service, six patients had received some medical help but proper diagnostic procedures and sufficient education on DSD had stayed out. From studies on hypospadias repair, we know there is an optimal time window for treatment; corrections performed in early childhood gives better urinary and sexual functioning than surgery performed after transition into adolescence (Woodhouse & Christie, 2005). The absence of differences between treated and untreated patients found in this study may be related to the fact that treatment had started lately. We assume that psychosexual problems such as dissatisfaction or shame for

an ambiguous genital may gradually develop prior to adolescence but may intensify in puberty when the body will develop into an ambiguity, visible for everybody and making the affected persons vulnerable for stigmatization. Since we could not test the impact of early treatment in childhood on psychosexual development among our patients, we have not able to assess effects of early treatment on sexual functioning and quality of life yet, but we hope we will be able to study this in the future.

Study limitations

Prior to the study, locally validated instruments were unavailable. We performed an exploratory study first by utilizing Indonesian translations of existing instruments developed in Western countries. We were well aware that application of Western measures could lead to different types of methodological problems and we found solutions to these problems so that we could reach our goal to gain insight in psychosexual problems in late treated Indonesian patients with DSD. First, we carried out a pilot study to found out the applicability of the measures. We then found out that it would be better to apply questionnaires orally to avoid misunderstandings by illiteracy or unfamiliarity with *Bahasa Indonesia*. Second, we compared data of patients with those of matched controls, and finally we applied a web based survey in a large group of healthy Indonesians to carry out reliability analyses and scale construction in the Indonesian population. Our analysis showed that the Indonesian translations had many similarities with the original measures and also had good psychometric properties. Therefore, we assumed that it was valid to apply the questionnaires in our study. However, it is true that the web-based participants differed from the patient and matched control groups by their socio-economic status; these group differences may limit the applicability of the validity and reliability measures to the experimental subjects.

Another limitation is that this study included different DSD diagnoses with a small number of patients in each diagnostic group. This hampered us to perform a more detailed comparison between patients with 46,XX karyotype and CAH or 46,XY karyotype and AIS or gonadal dysgenesis that had been raised in different gender. DSD is an umbrella term for many different anomalies in sexual development that covers a large variety in the underlying biological mechanisms leading to specific types of DSD. Part of the psychological distress is probably related to specific underlying biological mechanism of each

specific type of DSD so that in studies with small groups of patients only those psychological problems will appear that are most significant and are shared by patients in all diagnostic groups.

Our patients never had received or only had received little medical attention before they entered our hospital. We therefore were able to explore psychosocial and psychosexual problems faced by patients with DSD in whom the bodies and minds had developed without or with limited influences of medical treatment for DSD in most of their life. In the past 20 years, it has become clear that many patients with DSD experience psychosocial and psychosexual problems that need to be attended. Often early medical treatment has been pointed out as source of these psychosexual problems, and some activists groups ask for delay of all childhood treatments not necessarily needed for survival. Our findings demonstrate that psychosexual problems are also present in patients who did not receive treatment and that there are many similarities with the psychosexual and psychosocial problems faced by Indonesian untreated patients and Western treated patients. These similarities in experienced psychosexual and psychosocial problems indicate that the problems are related to DSD itself rather than initiated by early medical treatment. We think that the psychosocial problems of which Indonesian patients have to deal with are large, due to lack of understanding about DSD, particularly in the community, that complicated patients' ability to cope with body ambiguity. Improvement can be reached by early diagnosis followed by comprehensive education to the parents on the diagnosis and treatment possibilities, both hormonal and surgical, so that the patients and/or parents will be able to make informed choices that they consider will be best for their child (Warne & Raza, 2008). The child's wishes need to be taken into account as soon as the child is able to become involved in medical decision making. Medical treatment of DSD is complex and only should be performed by experienced, specialized, multidisciplinary teams.

Conclusion

Having a DSD condition, being infertile and fearing rejection caused significant distress, particularly among women. A non-exclusively heterosexual orientation in sexual attraction was more likely reported among adults with DSD than their matched controls. Late-treated patients experienced similar

problems to untreated patients. Health practitioners should be aware of the social implications of reduced infertility and sexual functioning among adults with DSD. Genetic counseling, patient education, and psychological counseling may provide support for patients and caregivers to discuss sexual problems, strategies for coping with the conditions, ultimately facilitating greater acceptance. We recommend that primary health care providers identify patients with DSD early in life and refer them to a specialized multidisciplinary team, so adequate intervention can be provided.

As the majority of our patients never had received medical attention before they entered our hospital, we had been able to study the course of development without medical treatment for the DSD and its impact on the psychosexual and psychosocial aspects of persons with DSD. By studying psychosexual functioning in untreated or late treated patients we have been able to explore the problems faced by patients with DSD in whom the bodies and minds had developed without or with limited medical intervention for their DSD for most of their life.

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Chapter 4

2

Gender development in Indonesian children, adolescents, and adults with disorders of sex development

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Abstract

In most Western countries, clinical management of disorders of sex development (DSD) starts immediately after diagnosis. For many Indonesian patients born with ambiguous genitalia, limited medical help had been available. Consequently, these patients have been raised with ambiguous genitalia or bodies. We investigated gender identity and gender role behavior in 118 Indonesian subjects (76 males, 41 females) with different DSD diagnoses in comparison with 118 healthy controls matched for gender, age, and residential setting (rural, suburban, or urban). In study 1, we report on methodological aspects of the study: scale adaptation, pilot testing, and validity/reliability of measured. In study 2 we report on gender outcome in 60 children (42 boys, 18 girls), 24 adolescents (15 boys, 9 girls), and 34 adults (19 men, 15 women) with DSD. The majority of patients never had received any medical treatment prior to this study. We observed a remarkably high percentage of gender change: 6.7% among children; 8.3% among adolescents; 44.1% among adults. All except one (95%) had changed gender from female to male. 81% had 46,XY karyotype, their bodies had undergone significant masculinization during life. Gender identity confusion and cross-gender behavior was more frequently observed in children with DSD raised as girls than in other groups. Adolescents and adults with DSD raised as females experienced more gender-related problems. Puberty and associated masculinization is critical for development of gender-related problem in individuals with 46,XY DSD raised as females. An integrated clinical and psychological follow-up on gender outcome is necessary during pre-puberty and adulthood.

KEYWORDS gender identity, gender role behavior, disorders of sex development, gender change, Indonesia

Introduction

Disorders of sex development (DSD) are characterized by an atypical development of the anatomical sex (Hughes, Houk, Ahmed, & Lee, 2006). Many individuals with DSD are identified at birth or in childhood because they have ambiguous or atypically developed genitalia. In others, the appearance of external genitalia is normal at birth. They will be identified in adolescence when the expected pubertal changes do not take place. In Western countries children with ambiguous genitalia or adolescents experiencing an atypical development in puberty will enter the medical services for a diagnostic work up, usually followed by advice and medical treatment.

In children with DSD born with ambiguous genitalia, gender will be assigned. In these children, the development of genital ambiguity is caused by hypervirilization (an excess of prenatal androgen production) or hypovirilization (insufficient androgen production or action). Experimental studies in animals have demonstrated that the development of masculine behavior is related to the action of prenatal and neonatal androgens in the brain. Except in individuals with the androgen insensitivity syndrome, increased levels of prenatal androgens will lead to masculine behavior, whereas low level of prenatal androgen will lead to feminine behavior later in life. This action of prenatal androgens on behavior is also observed in human beings, particularly among girls (Hines, 2011). Studies on displayed gender role behavior and interests in children raised as girls with 46,XX karyotype and congenital adrenal hyperplasia (CAH) revealed that these girls display more typical masculine behavior and favor activities that are generally preferred by boys (Beltz, Swanson & Berenbaum, 2011). There is a dose-response effect, girls who had higher levels of circulating prenatal androgens (reflected by the severity of masculinization of the external genital at birth), displayed more masculine behaviors than girls who had moderate levels of circulating prenatal androgens (Meyer-Bahlburg et al., 2006). Social influences seem of minor importance; girls with 46,XX CAH raised in different Western countries all display masculinized behavior (Berenbaum, 1999; Berenbaum, Duck & Bryk, 2000; Nordenström, Servin, Bohlin, Larsson, & Wedell. 2002; Slijper, 1984) and parental permissiveness does not influence displayed masculinized behavior (Pasterski, Geffner, Brain, Hindmarsh, Brook & Hines, 2005). Meyer-Bahlburg and his colleagues (2006) observed that, despite their masculinized gender role behavior, gender identity problems are not seen among girls with

46,XX karyotype and CAH aged 5-12. Observation studies in adult women have revealed that the large majority of patients with 46,XX karyotype and CAH raised as girls developed a female gender identity but a small group of women developed gender dysphoria and of these, some chose to continue their lives as men. The percentage of women who changed their gender was high compared to the rate of gender change in non-DSD individuals (Dessens, Slijper, & Drop, 2005).

Children raised as girls with 46,XY karyotype and partial androgen insensitivity syndrome (PAIS), a disorder in the biosynthesis of testosterone or with partial gonadal dysgenesis (PGD) also displayed more masculine behavior compared to non-affected children (Jürgensen, Hiort, Holterhus, & Thyen, 2007), suggesting that also in individuals with 46,XY karyotype prenatal levels of androgens circulating in the brain affect those brain areas related to sex-typical behavior and interests (Hines, 2011). Studies on gender identity revealed that gender dysphoria and social gender role change are seen in patients with PAIS (Mazur, 2005; Melo et al., 2003) and in patients with disorders of androgen biosynthesis (Cohen Kettenis, 2005; Mendonca et al., 1996, Reiner, 2005) after they start to masculinize in puberty. In contrast, women with 46,XY karyotype and complete androgen insensitivity syndrome (CAIS) who have a normal or high testosterone production but are completely insensitive to androgen action, develop a female gender identity (Hines, Ahmed, & Hughes, 2003). Findings in young Indian patients (Ammini et al., 2002; Gupta et al. 2010) showed similarities with findings in Western studies. No other investigations in Asian countries have been reported.

In Western patients with DSD, diagnostic work-up and treatment follows immediately after identification of DSD. In developing countries doctors see patients who seek medical services later in life (Warne & Raza, 2008). Many patients and parents will only consult a doctor after psychological or social problems with genital or body ambiguity have intensified. In Indonesia medical management for patients with DSD is characterized by limitations in health resources and by socio-cultural and legal barriers that restrict choice for individuals with DSD. Every Indonesian newborn must be assigned a female or male gender and has to be registered in the local civil registration office within 60 days after birth in order to obtain a birth certificate. A birth certificate is compulsory for school entry, obtaining a diploma, health insurance, and an ID card. Delayed birth registration or change of gender in the birth registry requires

a legal procedure in an Indonesian state court. In case of gender change, either due to DSD or a gender identity disorder, the court will request a medical review before reaching a decision that the requested gender change is permitted.

In 2010, the Indonesian Ulama Council (MUI) released its fatwa –a religious edict– to ban sex reassignment surgery without medical reason. 'Without medical reason' here refers to transsexualism. According to this fatwa, gender reassignment due to DSD is permitted within Islam sharia. Even if not all the sex reassignment surgical procedures had been carried out and the sex change had not yet been legalized by the court, the Islamic law would already regard a person in that stage as a person in the reassigned gender. The MUI also endorsed other parties, e.g. local parliaments, the Indonesian Medical Association (IDI), and the courts, to integrate this fatwa into the new regulation on gender re-assignment (Haryadi, 2010). The MUI also released a formal letter supporting a child with 46,XY karyotype and ambiguous genitalia diagnosed with DSD to undergo a female-to-male gender reassignment (Raharjo, 2013).

Parents of newborns with ambiguous genitalia often report difficulties with the birth registration of their child. For many parents there is no professional help available and the socio-cultural and legal barriers are substantial. Our team was often confronted by patients who suffered from emotional problems because they lived in an ambiguous body, experienced gender confusion or gender dysphoria or suffered from social stigmatization. The ambiguous body, ambiguous gender identity, and cross gender behavior often confused parents or the community so that the child's gender was reassigned by the parents or the community. The reported problems in gender confusion form the basis of this study. No study on gender development in Indonesian subjects with DSD has been reported before.

This study aimed to assess gender identity and gender role behavior in children, adolescents, and adults with DSD whose first presentation for medical assistance had been significantly delayed and to compare findings in this study to findings that are known from studies performed in Western society. We addressed the following research questions:

- Do Indonesian patients with DSD display more cross gender role behavior and experience more gender identity problems than matched control subjects?

- In Western patients, the observed variation in gender role behavior among patients with DSD has been explained by prenatal action of steroid hormones on the developing brain. Can similar patterns of variation in gender role behavior be found in Indonesian patients and can these patterns also be explained by prenatal action of steroid hormones?

Outline of the report

We report our studies in two parts. In study 1 we report scale adaptation, pilot study for gender assessment, validity and reliability studies of the measures applied in study 2. In study 2 we report outcomes on cross gender role behavior and gender identity in Indonesian children, adolescents, and adults with DSD. The findings from both studies will be discussed in one general discussion.

Methods

The study protocol was approved by the board of the ethical committee from the Faculty of Medicine, Diponegoro University, Semarang, Indonesia.

Study 1: Scale adaptation and pilot study for gender assessment

Prior to this study, no relevant measures was available in the local language (*Bahasa Indonesia*). Therefore we used measures developed in Western countries that had been applied in comparable studies. This enabled us to compare findings in our study with findings reported in Western studies.

Method

The scale adaptation was conducted through the following stages: translation into local language (*Bahasa Indonesia*) by a certified translator, panel review on the Indonesian translations of measures by involving local researchers and an anthropologist who had vast expertise on gender studies in Indonesian culture and understands both English and Indonesian languages, and a pilot study involving healthy subjects and patients with DSD to evaluate the applicability of the measures. To assess validity and reliability on measures applied in children and adolescents, data were obtained from patient and

matched control samples. Their characteristics are described in Study 2. To assess validity and reliability of measures applied in adults, we conducted a web-based survey to involve a large group of participants.

Participants and procedures

Pilot study participants. Thirty-six subjects, aged 6-25 years, male or female, were recruited for the pilot study group, which comprised six patients (two adults, two adolescents, two children) and 30 healthy subjects (10 children, 10 adolescents, 10 adults). The healthy subjects, from different socioeconomic backgrounds, were contacted through the *Pak Lurah* (local leader) and joined the study voluntarily. Oral and written study information was given by the researcher (AE). After the adult participants and parents of subjects under age 18 had given their consent, questionnaires were administered in a similar procedure for patients and matched controls to study the applicability of the initial protocol. The participants received a gift (stationery or towel) in thanks for their participation.

To assess the validity and reliability of the measures applied in the child and adolescent samples, we used data from 120 children (60 children with DSD and 60 matched controls children) and 48 adolescents (24 adolescents with DSD and 24 matched control adolescents) who participated in Study 2. This group, for the study on psychometric quality, comprised 84 boys and 36 girls aged 6-11 and 30 adolescent boys and 18 adolescent girls aged 12-17.

Web-based survey participants. The web-based survey was set up in the local language (*Bahasa Indonesia*). During a four-week period, invitations to participate in the web-based survey were emailed to mailing lists of Indonesian communities (i.e. university students, university graduates, Indonesian professionals' networks). Snowball recruitment was applied: recipients were encouraged to forward the email invitation to their adult contacts. Study information e.g. the study aim, the principal investigator and affiliations, the estimated time needed to complete the self-report, and confidentiality assurance were provided on the welcome page prior to participation. Visitors to the web-survey page could give informed consent by ticking off a box and then respond to the survey. Alternatively, they could decline participation. They were not obliged to answer all questions. In total, 377 healthy Indonesian adults aged 18-45 joined the web-based study. Of 377 participants, 316 adults completed the Gender questionnaire and 254 adults completed the Activities questionnaire.

Measures

To assess gender identity and gender role behavior in children, we applied the Gender Identity Interview for Children (GIIC) and the Gender Identity Questionnaire on Children (GIQC). Both measures had been have used in studies in children with reported gender identity disorders across nations (Zucker et al., 1993; Wallien et al., 2009). For adolescent and adult samples, we applied the Gender Questionnaire and the Activities Questionnaire, both measures had been applied in studies involving patients with androgen insensitivity syndrome (AIS) (Hines et al., 2003) and CAH (Hines et al., 2004).

Gender Identity Interview for Children (GIIC). The Gender Identity Interview for Children (GIIC) measures children's reports on gender identity as in affective and cognitive gender confusion (Zucker et al., 1993) and has been applied in the Dutch and North American population for international comparison (Wallien et al., 2009). In the original English language version, this scale consists of 12 items and is designed to assess gender identity disorder in children. Each item is provided with a 3-options response mode ranging from 0-2: in line with biological sex (score 0), ambiguous or intermediate response (score 1), and opposite of biological sex (score 2). In this study, we added one question referred to liking or disliking the external genitalia. In the version for boys, the question was: "If you stand in front of the mirror, which part of your body you like the most?" subsequently leading to different body parts and the genital. A 3-options response mode was applied: *male genital*, *neither male nor female genital*, *female genital*. The opposite-sex terms were applied for the girls' version. Higher scores indicate more gender confusion.

Gender Identity Questionnaire for Children (GIQC). The Gender Identity Questionnaire for Children (GIQC) assesses a parent's evaluations of their child's gender role behavior and cross gender role behavior (Johnson et al., 2004). This Likert rating scale consists of 16 items with a 5-options response mode measuring frequencies of various sex-typical behaviors (ranging from *never* to *always*). Lower scores indicate more frequent cross-gender role behavior. This measure has been applied internationally in order to assess gender dysphoria in children (Cohen-Kettenis et al., 2006).

Gender Questionnaire. The Gender Questionnaire aims to assess the individual's core gender identity, gender role behavior, and sexual orientation (Hines et al., 2003). For this study, we only used eight items measuring gender identity and gender role behavior (items 1-8). We added the following questions

to assess subjects' wishes for a social gender role change (in the version of women): *"I was treated as a man by people who knew me well and people who were unfamiliar to me"*, *"I present myself as a man during work or leisure time"*, *"I want medical treatment to change the appearance of my body into a man's body"*. Two reference periods were applied for each additional item: in the past 12 months and during lifetime. In the male version, similar questions were applied by replacing the term "man" with "woman". In total, six items were added for the purpose of this study; therefore the Indonesian version of Gender Questionnaire comprised 14 items. We provided two versions (female and male version) to the participants based on the gender they lived in at participation in the study. Similar to the original English version, a seven-option response mode ranging from *always* (1) to *never* (7) was used and reversed scoring was applied in items 5-14.

Activities Questionnaire. The 14-item Activities Questionnaire measures the recalled childhood preferences for playmate, toys, or activities (Hines et al., 2003). Following the original version, a five-option response mode ranging from *almost always* (1) to *not at all* (5) was applied to assess stereotypically masculine, feminine, or neutral preferences, except in one question assessing preference for playmate that ranged from *always girls* (1) to *always boys* (5). Similar to the original scale, reversed scoring was applied in negatively worded items, therefore higher scores reflecting greater preferences in sex-typical preferences.

Statistical analysis for assessing validity and reliability

The construct validity was explored using principal component analysis (PCA) with varimax rotation method and Kaiser normalization. Factors with Eigen values greater than 1 and items with factor loadings greater than .40 were considered acceptable. Instrument reliability was evaluated as internal consistency, with Cronbach's Alpha as outcome measure. Several models were tested; here we report the optimal model for the Indonesian data.

Results

Validity and reliability of measures. During the pilot we learned that participants were willing to discuss gender-related issues; the paper-pencil methods in administering the measures was only effective for better educated

participants who were also familiar with self-report methods. For participants who received limited education or were illiterate and participants who were unfamiliar with self-reports, oral application was the best way to apply measures. Oral application ensured participants understood the questions before they gave an answer. The results of principal component analysis (PCA) and reliability analysis (Cronbach alpha for internal consistency) are summarized in Table 1.

Table 1 Results of principal component analysis (PCA) and reliability analysis of measures used in the study

Measures (number of items applied in this study)	N	Number of components (% of total variance explained)	Components and item distributions	Cronbach's alpha (α)
Gender Identity Interview for Children / GIIC (9 items)	120	2 PC (71.7) 1 PC (56.8)	- Cognitive gender confusion (items 1, 2, 6, 8, 10) - Affective gender confusion (items 3, 5, 7, 11) Overall gender confusion (9 items)	.78 .86 .88
Gender Identity Questionnaire for Children / GIQC (10 items)	120	1 PC (37.3)	Child's gender role behavior (parent report)	.88
Gender Questionnaire (14 items)	316	2 PC (74.9)	Gender identity and gender role behavior (items 1-4) Cross-gender identity and cross-gender role behavior (items 5-14)	.88 .96
Activities Questionnaire / Recalled childhood preference (12 items)	254	3 PC (55.2)	Masculine type of preference (items 1, 3, 4, 5, 7) Feminine type of preference (items 2, 10, 12) Neutral type of preference (items 6, 8, 9, 11)	.87 .73 .38

Table 2 Mean, standard deviation, and factor loadings after varimax rotation of the Indonesian version of GIIC items

Items (Boy version)	*M* ± SD	Factor loadings (2 PC)		Factor loadings (1 PC)
		Factor 1[a]	Factor 2[b]	
1. Are you a boy or a girl?	.02 ± .18	**.91**	.12	.81
2 (3). When you grow up, will you be a Mommy or a Daddy?	.04 ± .27	**.76**	.19	.72
3 (5). Are there any good things about being a boy?	.08 ± .35	.43	**.77**	.81
*4 (6). Are there anything you don't like about being a boy?)	NA	NA	NA	NA
5 (7). Do you think it is better to be a boy or a girl?	.08 ± .35	.45	**.82**	.85
6 (8). In your mind, do you ever think that you would like to be a girl?	.08 ± .36	**.59**	.47	.76
7 (9). In your mind, do you ever get mixed up and you are not really sure if you are a boy or a girl?	.13 ± .44	-.13	**.76**	.35
8 (10). Do you ever feel more like a girl than like a boy?	.06 ± .27	**.82**	.20	.78
*9 (11). You know what dreams are, right? When you have a dream at night, are you ever in the dream? If yes, ask: in your dreams, are you a boy, a girl, or sometimes a boy and sometimes a girl?)	NA	NA	NA	NA
10 (12). Do you ever think that you really are a girl?	.03 ± .22	**.83**	.22	.80
**11. If stand in front of the mirror, which part of your body you like the most?	.07 ± .31	.47	**.69**	.79

Note. *M* = mean; SD = standard deviation. Number in the brackets refers to numbering applied in the original version of the GIIC.

* These items were applied in the study but were not included in the principal component analysis and reliability analysis due to large proportion of missing data (NA = not applicable). ** This item was added for this study.

In Zucker et al. (1993), items 1 and 2 above were loaded onto the cognitive gender confusion factor, whereas items 4-10 above were loaded onto the affective gender confusion factor. In Wallien et al. (2009) items 1-10 above loaded into single factor of gender confusion.

In our study, factor 1 = cognitive gender confusion; factor 2 = affective gender confusion. Cronbach's alphas of the factor 1, factor 2, and single factor of the Indonesian version of GIIC are: .78; .86; .88, respectively. N = 120.

Gender Identity Interview for Children (GIIC). During the pilot study, we revealed three problematic items in the Indonesian translation of GIIC: item 2 ("Are you a ….?" –a boy or a girl opposite to first response given), item 4 ("Could you ever grow up to be …?" –a boy or a girl opposite to first response given), and item 11 that assess personae in dreams (numbering according to the original scale). Item 2 and item 4 triggered unexpected responses from children (laughing or upset) and/or parents (irritated or suspicious) which reduced children's or parents' enthusiasm to respond to further questions.

Regarding item 11, most of the children reported to never have had dreams or dreamed about ghosts without any indication to the ghost's gender. Their parents confirmed the children's reports as their children favored a very popular reality TV show about ghosts. We considered the influence of a culture-bias in these items. After reviewing these problematic items, we decided not to apply items 2 and 4, but applied item 11 carefully to see the possibility of different findings reported from study participants. Consequently, the item numbering differed from the original English version (see Table 2 for items applied in this study).

During the study, we identified two items with a low response rates: item 6 ("Are there anything you don't like about being a boy?" - question given to a boy) and item 11 assessing child-reported dream (item numbers according to the original scale). Due to the large proportion of missing data (55-98%), we excluded these items from statistical analyses and subsequently performed PCA and internal consistency analysis on the nine remaining items. The PCA generated two PC solutions and 71.66% of the total variance was explained. All items had a factor loading greater than .60. Table 2 showed item 1, 2, 6, 8, 10 were loaded to factor 1, whereas item 3, 5, 7, 11 were loaded to factor 2 (item numbering according to the version applied in this study). Although factor 1 reflects the cognitive component of gender confusion and factor 2 mirrors affective component of gender confusion, item loaded differently on each of the principal component compare to previous studies (Zucker et al., 1993; Wallien et al., 2009). The PCA extracted a single factor model that explained 56.8% of the total variance. The Cronbach's alphas obtained for factor 1 (α = .78), factor 2 (α = .86), and all nine items together (α = .88) indicated that the Indonesian version of GIIC has a good internal consistency. For this study, we applied the single factor 9-item model of the GIIC (total score range between 0 = no gender confusion, and 18 = extreme gender confusion).

The Parent-report Gender Identity Questionnaire for Children (GIQC). Analysis of the Indonesian version of GIQC showed that the response rates of the items 9 and 12 (original items number) were only 16.7-21.7%. This suggested that the role-play (item 9) and the dress-up games (item 12) were unpopular activities among subjects. In view of the large non-response rates, these two items were excluded and the PCA was performed in 11 items of the Indonesian version of GIQC and generated a one PC solution that explained 37.34% of the total variance. Table 3 shows the factor loadings of each item obtained in this study in comparison to previous studies on GIQC.

Table 3 Mean, standard deviation, and factor loadings after varimax rotation of the GIQC items

Original item number	$M \pm SD$ (current study)	Factor loadings reported in studies using GIQC		
		Current study	Johnson et al (2004)	Elizabeth et al (1984)
1. Playmate	3.9 ± 1.0	.62	.77	.80
2. Girl's doll	4.3 ± 1.3	.71	.74	.77
3. Boy's doll	4.3 ± 1.2	.70	.34	.30
4. Make-up	4.3 ± 1.3	.80	.71	.77
5. Imitate female model	4.0 ± 1.6	.75	.64	.69
6. Imitate male model	3.0 ± 1.8	-.47	.48	.59
7. Play sports with boys	4.1 ± 1.2	.69	.62	.67
8. Play sports with girls	4.1 ± 1.2	.63	.20	.38
*9. Role play	NA	NA	.89	.92
10. Girl's type play	4.5 ± 1.0	.84	.83	.88
11. Boy's type play	4.4 ± 0.9	.80	.72	.85
*12. Dress-up games	NA	NA	.91	.94
*13. Wishes to be the opposite-sex	4.9 ± 0.5	.36	.81	-
*14. Stated own self as the opposite-sex	4.9 ± 0.6	.23	.69	-
*15. Disliking own sexual parts	4.7 ± 0.7	-.09	.47	-
*16. Liking own sexual parts	1.2 ± 0.7	-.01	.02	-

Note. N = 120. *M* = mean; SD = standard deviation. NA = not applicable.
* These items were not applied in this study. Items 9 and 12 had a large missing response; items 13-16 had poor factor loadings. The remaining 10 items (items 1-8, 10, 11) were applied in this study.

The majority of items had similar or higher factor loadings compared to previous studies (Elizabeth & Green, 1984; Johnson et al., 2004), except four items (items 13-16) that had very low factor loadings. One item (item 6) had a negative factor loading indicating that reversed scoring was needed; however this item remained problematic in the reliability analysis. Therefore we excluded this item for further analysis. Internal consistency of the remaining 10 items resulted in a Cronbach's alpha = .88 indicating that the Indonesian version of GIQC has a good reliability. The total score of GIQC ranged from 5 to 50. Low scores indicate that parents report frequent cross-gender behavior in their child.

Gender Questionnaire. PCA generated two components explaining 74.9% of total variance. Table 4 shows that items 1-4 loaded on factor 1 and reflected *gender identity and gender role behavior*. Items 5-14 loaded on factor 2 and reflected *cross-gender identity and cross-gender role behavior*. The Cronbach's alphas of both factors indicate good internal consistency ($\alpha = .88$; $\alpha = .96$, respectively). The results were summarized in two sum scores for *gender identity and gender role behavior:* in the past 12 months and during lifetime (range sum

score: 2-14 for each period) and two sum scores for *cross-gender identity and cross-gender role behavior:* in the past 12 months and during lifetime (range sum score: 5-35 for each period). Low scores on gender identity and gender role behavior (factor 1) indicate a distinct sex-typical gender identity and gender role behavior in the specified periods. Higher scores on cross-gender identity and cross-gender role behavior (factor 2) indicate a cross-gender identity and more cross-gender role behaviors.

Activities Questionnaire. During the pilot study, two problematic items were identified: items 13 (degree of girlishness) and item 14 (degree of boyishness). Due to the absence of appropriate equivalents in local language, we used the terms feminine and masculine. However, all subjects perceived being feminine or masculine referred to having an ideal female or male appearance (as models in commercials). Consequently these items lack of sensitivity to determine the degree of femininity or masculinity. We decided to exclude these items from further statistical analyses. PCA was performed on the remaining 12 items generated three components of preference explaining 55.2% of total variance. Table 5 shows that items 2, 10 and 12 loaded on factor 1 assessing feminine type of preferences; items 1, 3, 4, 5, 7 loaded on factor 2 assessing masculine type of preferences and items 6, 8, 9, 11 loaded on factor 3 assessing neutral type of preferences. Cronbach's alphas were: feminine: $\alpha = .87$; masculine: $\alpha = .73$; and neutral: $\alpha = .38$. As the neutral scale had poor internal consistency, we report the masculine and feminine scales only. To allow a valid comparison, following the original scoring procedure, the sum score of the feminine scale was multiplied by 1.67 prior to comparison (Hines et al., 2003). The sum score range was 5-25 for the feminine and masculine components. Higher scores indicate greater preferences for typical feminine or masculine activities as recalled by the subjects.

Table 4 Median, range, and factor loadings of the Gender questionnaire items

Items	Median	Range	Factors	
			1	2
1. During the *past 12 months*, my behavior has been what most people consider appropriate for my sex	1.0	6	.17	**.90**
2. During *my lifetime*, my behavior has been what most people consider appropriate for my sex	1.0	6	.11	**.91**
3. During *the past 12 months*, I enjoyed being a person of my sex	1.0	6	.39	**.66**
4. During *my lifetime*, I enjoyed being a person of my sex	1.0	6	.39	**.72**
5. During *the past 12 months*, I have wished I were a person of the opposite sex	1.0	6	**.76**	.31
6. During *my lifetime*, I have wished I were a person of the opposite sex	1.0	6	**.67**	.47
7. During *the past 12 months*, I have thought I was psychologically a person of the opposite sex	1.0	6	**.82**	.37
8. During *my lifetime*, I have thought I was psychologically a person of the opposite sex	1.0	6	**.76**	.45
9. During *the past 12 months*, I have been treated as person of the opposite sex by people who knew me well and people who were unfamiliar to me	1.0	6	**.73**	.39
10. During *my lifetime*, I have been treated as person of the opposite sex by people who knew me well and people who were unfamiliar to me	1.0	6	**.68**	.48
11. During *the past 12 months*, I have presented myself as person of the opposite sex at my job and during leisure time	1.0	6	**.84**	.26
12. During *my lifetime*, I have presented myself as person of the opposite sex at my job and during leisure time	1.0	7	**.82**	.30
13. During *the past 12 months*, I wanted medical treatment to change my body into a body of the opposite sex	1.0	6	**.90**	.08
14. During *my lifetime*, I wanted medical treatment to change my body into a body of the opposite sex	1.0	7	**.92**	.09

Note. N = 316. Factor loadings represent factor loading after varimax rotation. Factor 1 = Gender identity and gender role behavior; Factor 2 = Cross-gender identity and cross-gender role behavior. Items 1-8 were obtained from the original version of the Gender Questionnaire (Hines et al., 2003); items 9-14 were added for this study. The Cronbach's alphas for both factors above are .88 and .96, respectively.

Table 5 Mean, standard deviation, and factor loadings of the Activities Questionnaire items

Items	*M* ± SD	Factor loadings		
		Feminine	Masculine	Neutral
1. (Male) Playmate	3.1 ± 0.9	-.47	**.47**	.12
2. Dolls	3.0 ± 1.2	**.79**	-.20	-.13
3. Sports	3.6 ± 0.9	.03	**.67**	-.12
4. Cars	3.3 ± 1.1	-.60	**.49**	-.20
5. Play outside	4.1 ± 0.7	-.05	**.75**	.005
6. Drawings	2.7 ± 1.0	.001	-.05	**.71**
7. Rough-tumble play	2.6 ± 1.2	-.40	**.65**	-.11
8. Reading	1.7 ± 0.7	-.14	.28	**.50**
9. Board games	1.9 ± 0.7	-.34	-.14	**.37**
10. Dress-up	2.6 ± 1.2	**.88**	.01	-.02
11. Building blocks	2.4 ± 0.9	.06	-.28	**.66**
12. Cosmetics	2.4 ± 1.2	**.88**	-.11	-.09

Note. N = 254. *M* = mean; SD = standard deviation. Factor loadings represent factor loadings after varimax rotation. Items 13 and 14 in the original measure (Hines et al., 2003) were problematic therefore both items were not included for PCA and reliability analysis. The Cronbach's alphas of the Indonesian version of Activities Questionnaire for the feminine, masculine, and neutral factors are .73; .87; .38 respectively.

Study 2: Gender identity and gender role behavior in patients with DSD

Study design

Comparison between patients with DSD and healthy control subjects matched for gender, age, and residential settings (rural, suburban, or urban area).

Participants

Patients with DSD. The study comprised 118 patients diagnosed with DSD: 60 children (42 boys, 18 girls; aged 6-11), 24 adolescents (15 boys, nine girls; aged 12-17), and 34 adults (20 men, 14 women; aged 18-41). Inclusion criteria were: individuals born with a DSD condition aged 6 years or older. Despite extensive analysis, a molecular diagnosis was made in only 16 out of 57 (28.1%) patients with 46,XY karyotype and hypomasculinization. In these patients a mutation in the androgen receptor gene (AR gene) had been found leading to the diagnoses of complete and partial androgen insensitivity syndromes (CAIS and PAIS). Patients in whom no molecular diagnosis was found fell into the following categories: (1) androgen action disorder (AAD), referring to patients with 46,XY karyotype and undermasculinization with hormonal observations close to androgen insensitivity syndrome or a disorder in the biosynthesis of testosterone; (2) undermasculinization unknown cause refers to patients with

46,XY karyotype in whom the underlying cause of undervirilization remained unknown. Patients with 46,XX karyotype and the simple virilizing type of CAH or cloacal malformation are also included in the study. We excluded individuals with 46,XY and 46,XX DSD and features suggestive of a dysmorphic syndrome, patients with sex chromosome DSD without mosaicism, and patients with DSD and intellectual disabilities (indicated from parent reports on their child's academic achievements and/or observed by the medical doctor in interaction with the patient). Of the 168 patients who matched the inclusion criteria, 21 patients (12.5%) were lost to follow-up due to relocation or invalid contact details, and 29 patients (17.3%) declined to participate. The majority of patients who declined participation were children (51.7%) who were predominantly male (64.3%) and who had been diagnosed with 46,XY androgen action disorder (37.9%). Table 6 presents the diagnostic characteristics, the reported treatment already received and the gender history of all 118 patients who participated in this study. With respect to applied questionnaires on gender role behavior and gender identity, assessment was done according to the gender in which the patient was living at the time of their participation in the study.

Sixty-one patients (51.7%) had received some surgical or hormonal treatment. In general, Indonesian patients are informed orally by their doctors. Doctors hardly ever exchange written medical information. As a consequence, little is known about past medical examinations, medical diagnostic procedures or medical and surgical treatments. Reports on surgical treatments that were received are summarized in Table 6. The remaining 57 patients (48.3%) had not received any medical evaluation or treatment prior to this study. The study included 11 children with 46,XX karyotype and CAH-SV who had been raised as girls and who had received some hormonal treatment. Hormonal therapy often had been taken irregularly because medication was generally unavailable or for the family, unaffordable. There was one boy with 46,XX karyotype and CAH-SV who had received hormonal treatment for 9 months in infancy, then irregularly received treatment when he was aged 6, and was left untreated in at least two years prior to this study (S10; Table 6). Two boys diagnosed with gonadal dysgenesis (aged 6; S21; Table 6) and PAIS (aged 9; S32; Table 6) received HCG injections in periods of one and four years before this study. Twelve girls and 17 boys with different diagnoses (aged 6-11) had undergone genital surgery. The girls were younger at their first surgery than the boys (mean age ± SD for girls: 4.7 ± 2.0 years; for boys 5.2 ± 2.4 years). Twelve boys and two girls had undergone multiple genital surgeries.

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118)

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
Children (S01-60)													
S01	6	46,XX	CAH-SV [a]	3	2.8	6	3	F	None	F	F→M (age 2-3)	M	Gradually. Self-initiated gender change. Sibling of S86 and S87.
S02	6	46,XX	CAH-SV [a]	3	4.5	4	4	F	Hydrocortisone since age 3.	F	F	F	No
S03	6	46,XX	CAH-SV [a]	6	4	4	4	F	Clitoridoplasty age 6, Hydrocortisone since age 6.	F	F	F	No
S04	6	46,XX	CAH-SV [a]	4	4	7	4	F	Hydrocortisone since infancy; clitoridoplasty age 5.	F	F	F	No
S05	6	46,XX	CAH-SV [a]	6	4.5	4	4	F	Hydrocortisone since age 4 (other clinic).	F	F	F	No
S06	7	46,XX	CAH-SV [a]	2 months	2.5	4	4	F	Hydrocortisone since age 3.	F	F	F	No
S07	8	46,XX	CAH-SV [a]	4	4.1	4	4	F	Medication at birth (other clinic; details unknown); clitoridectomy age 5.	F	F	F	No
S08	8	46,XX	CAH-SV [a]	2	3	4	3	F	Hydrocortisone since age 1; clitoridectomy age 2.	F	F	F	No
S09	8	46,XX	CAH-SV [a]	8	4.3	4	4	F	None	F	F	F	No
S10	8	46,XX	CAH-SV [a]	8	6	4	5	M	Hydrocortisone irregularly since infancy.	M	M	M	No
S11	8	46,XX	CAH-SV [a]	8	5.5	3	3	M	None	M	M	M	No
S12	9	46,XX	CAH-SV [a]	7	4.5	4	4	F	None	F	F	F	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S13	10	46,XX	CAH-SV [a]	6	4.5	4	3	F	Hydrocostisone irregularly at infancy; regularly since age 4; Clitoridoplasty age 7.	F	F	F	No
S14	11	46,XX	CAH-SV [a]	7	5	4	4	F	None	F	F	F	No
S15	11	46,XX	CAH-SV [a]	11	3	7	4	F	Clitoridectomy age 2; hydrocortisone since age 11.	F	F	F	No
S16	11	46,XX	CAH-SV [a]	11	normal clitoris	1	3	F	None	F	F	F	No
S17	11	46,XX	CAH-SV [a]	11	normal clitoris	4	2	F	Clitoridectomy age 4 (other clinic).	F	F	F	No
S18	11	46,XX	CAH-SV [a]	11	3.5	4	3	F	Clitoridoplasty age 8 (other clinic) and 11; hydrocortisone age 11.	F	F	F	No
S19	7	46,XX /47,XXY	Chromosomal DSD [b]	1	3	9	(4)	M	None	M	M	M	No
S20	7	46,XX /46,XY	Chromosomal DSD [b]	7	3	8.5	(4)	M	None	M	M	M	No
S21	9	46,XY /46,XX	Chromosomal DSD [b]	4	3.5	6	(2)	M	Orchidectomy age 4; HCG injection age 5	M	M	M	No
S22	6	46,XY	GD [c]	2	2	5	(2)	M	None	M	M	M	No
S23	6	46,XY,r (Y)/ 45,X	GD [c]	2	1.5	6	(2)	M	Surgery once (details unknown)	M	M	M	No
S24	6	46,XY	GD [c]	5	3	5	(3)	M	Chordaectomy age 5; Urethroplasty age 6	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S25	7	46,XY /45,X	GD [c]	2	1.7	1	(4)	F	Vaginoplasty, orchidectomy age 4	F	F	F	No
S26	7	46,XY	GD [c]	3	3	9	(3)	M	Surgery age 2 (details unknown; other clinic)	M	M	M	No
S27	8	46,XY	GD [c]	7	3.5	3	(3)	F	None	F	F→A	A	Male gender reassign-ment after the study.
S28	9	4 6 , X Y / 45,X	GD [c]	9	4	5	(3)	M	None	M	M	M	No
S29	10	46,XY	GD [c]	10	normal clitoris	1	(6)	F	None	F	F	F	No
S30	11	46,XY	GD [c]	10	4.5	6	(2-3)	M	None	M	M	M	No
S31	6	46,XY	PAIS [d]	2	2	6	(2)	M	Surgery (details unknown)	M	M	M	No
S32	6	46,XY	PAIS [d]	5	2.5	7	(3)	M	HCG injection age 5	M	M	M	No
S33	10	46,XY	PAIS [d]	4	4.9	10	(2)	M	None	M	M	M	No
S34	10	46,XY	PAIS [d]	10	4.5	6.5	(4)	M	None	F	FM (age 3)	M	Gender reassign-ment (parents)
S35	11	46,XY	PAIS [d]	11	4.5	6	(3)	M	None	M	M	M	No
S36	6	46,XY	AAD [e]	1	2	6	(3)	M	Hypospadia correction twice, urethroplasty age 2	M	M	M	No
S37	6	46,XY	AAD [e]	3	2	6	(3)	M	Hypospadia corrections three times (details unknown)	M	M	M	No
S38	6	46,XY	AAD [e]	4	3	5	(2)	M	Chordaectomy, orchidopexy age 4; urethroplasty age 5	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S39	6	46,XY	AAD [e]	6	3	6	(3)	M	None	M	M	M	No
S40	7	46,XY	AAD [e]	2	3.7	5.5	(4)	F	None	F	F→M (age 2)	M	Gender reassignment
S41	8	46,XY	AAD [e]	7	3	4	(2)	M	None	M	M	M	No
S42	8	46,XY	AAD [e]	3	3	6	(2)	M	Chordaectomy age 2; urethroplasty age 3 and 4 (other clinic)	M	M	M	No
S43	9	46,XY	AAD [e]	9	3	6	(3)	M	None	M	M	M	No
S44	10	46,XY	AAD [e]	7	2	6	(3)	M	Urethroplasty, chordaectomy, age 7 and 10	M	M	M	No
S45	10	46,XY	AAD [e]	8	2.5	6	(3)	M	Surgery age 9 and 10 (details unknown)	M	M	M	No
S46	11	46,XY	AAD [e]	7	3	6	(3)	M	Orchidopexy age 7	M	M	M	No
S47	11	46,XY	AAD [e]	11	3.5	6	(4)	M	None	M	M	M	No
S48	11	46,XY	AAD [e]	11	4	6	(3)	M	None	M	M	M	No
S49	6	46,XY	Undermas-culinization e.c.i.[f]	2	4	9	(3)	M	Surgery twice (details unknown; other clinic).	M	M	M	No
S50	6	46,XY	Undermas-culinization e.c.i.[f]	5	3	9	(3)	M	Chordaectomy, urethroplasty age 5	M	M	M	No
S51	6	46,XY	Undermas-culinization e.c.i.[f]	6	2.4	9	(2)	M	None	M	M	M	No
S52	7	46,XY	Undermas-culinization e.c.i.[f]	7	3	9	(2)	M	None	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S53	8	46,XY	Undermasculinization e.c.i.[f]	3	3	10	(2)	M	None	M	M	M	No
S54	9	46,XY	Undermasculinization e.c.i.[f]	4	2.5	9	(3)	M	Hypospadia correction age 6	M	M	M	No
S55	9	46,XY	Undermasculinization e.c.i.[f]	6	3	9	(2)	M	None	M	M	M	No
S56	9	46,XY	Undermasculinization e.c.i.[f]	6	3 (low position)	10	(3)	M	Surgery age 6, 7, 8 (details unknown)	M	M	M	No
S57	9	46,XY	Undermasculinization e.c.i.[f]	9	2.7	10	(3)	M	None				No
S58	9	46,XY	Undermasculinization e.c.i.[f]	8	3.5	9	(3)	M	None	M	M	M	No
S59	10	46,XY	Undermasculinization e.c.i.[f]	7	4	9	(3)	M	Hypospadia correction age 4, 6, 7.	M	M	M	No
S60	10	46,XY	Undermasculinization e.c.i.[f]	9	3.5	9	(3)	M	Chordaectomy age 9.	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
Adolescents (S61-84)													
S61	12	46,XX	CAH-SV [a]	12	normal clitoris	1	3	F	Clitoridectomy age 3 (other clinic).	F	F	F	No
S62	16	46,XX	CAH-SV [a]	16	normal clitoris	1	2	F	Clitoridectomy age 7 (other clinic).	F	F	F	No
S63	13	46,XX	Cloacal malformation [g]	12	1.9	1	0	F	Colostomy repair one day after birth.	F	F	F	No
S64	13	46,XY /45,X	GD [c]	12	3	8	(2)	M	Hypospadia correction, gonadectomy age 12.	M	M	M	No
S65	13	46,XY	GD [c]	12	4.1	8	(3)	F	None	F	F	F	No
S66	14	46,XY /45,X	GD [c]	10	3.2	10	(1)	M	None	M	M	M	No
S67	14	46,XY /45,X	GD [c]	13	4	8	(2)	M	Chordectomy age 13.	M	M	M	No
S68	15	46,XY	GD [c]	15	6.5	8	(2)	M	None	F	F→M	M	Doubt own gender at age 12. Self-initiated gender change.
S69	17	46,XY	GD [c]	13	Normal clitoris	1	(6)	F	Gonadectomy age 10 (other clinic); Estrogen supplement since age 13.	F	F	F	No
S70	17	46,XY	GD [c]	17	5	4	(4)	F	None	F	F	F	No
S71	16	46,XY	CAIS	16	Normal clitoris	1	(6)	F	None	F	F	F	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S72	12	46,XY	PAIS [d]	5	1.5	7	(4)	M	None	M	M	M	No
S73	12	46,XY	PAIS [d]	9	3	5	(3)	F	None	F	F	F	No
S74	13	46,XY	PAIS [d]	12	3.1	6	(3)	M	None	M	M	M	No
S75	15	46,XY	PAIS [d]	12	3.1	6	(5)	M	Testosterone injection, gynecomastia age 13; hydrocele surgery age 14	M	M	M	No
S76	12	46,XY	AAD [e]	12	5	6	(3)	M	None	M	M	M	No
S77	13	46,XY	AAD [e]	13	5	6	(3)	M	Chordectomy age 5, 6	M	M	M	No
S78	14	46,XY	AAD [e]	14	3.2	7	(3)	M	Surgery age 4 (details unknown); chordectomy, urethroplasty age 14	M	M	M	No
S79	14	46,XY	AAD [e]	10	3	5	(2)	M	Urethroplasty age 8	M	M	M	No
S80	17	46,XY	AAD [e]	12	7.1	6,5	(3)	F	None	F	F→A (age 18)	A	Male gender reas-sign-ment after the study.
S81	17	46,XY	AAD [e]	14	6.5	6	(2)	M	Hypospadia correction age 15	M	M	M	No
S82	13	46,XY	Undermas-culinization e.c.i.[f]	8	4	9	(2)	M	Surgery (details unknown)	M	M	M	No
S83	14	46,XY	Undermas-culinization e.c.i.[f]	9	5.2	9	(2)	M	Chordectomy, hypospadia correction age 10 and 11	F	F	F	No
S84	15	46,XY	Undermas-culinization e.c.i.[f]	14	5	9	(2)	M	Chordectomy age 14, urethroplasty age 15	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
Adults (S85-118)													
S85	18	46,XX	CAH-SV [a]	11	3.6	4	3	F	Clitoridectomy age 16; Hydrocortisone	F	F	F	No
S86	22	46,XX	CAH-SV [a]	17	7	4	5	M	None	F	F→M (age 2-3)	M	Gradually. Self-initiated. CAH identified in adulthood. Sibling of S01 and S87.
S87	24	46,XX	CAH-SV [a]	24	5	7	5	M	None	F	F→M (age 2-3)	M	Sibling of S01 and S86. See remarks S86.
S88	36	46,XX	CAH-SV [a]	33	3.6	4	3	F	Clitoral reduction age 34; Prednisone since age 36.	F	F	F	No
S89	18	46,X i(X) (q10)/45,X	Chromosomal DSD [b]	18	Normal clitoris	1	0	F	None	F	F	F	No
S90	20	46, X, i(X) (q10) (85%) / 45, X (15%)	Chromosomal DSD [b]	20	Normal clitoris	1	0	F	Pills (unknown; to get menstruation) age 20; Dianne35 pills	F	F	F	No
S91	29	45X (99%) / 46 XX,iXq	Chromosomal DSD [b]	25	Normal clitoris	1	0	F	Cycloprogynova age 23; Profertil, Zumenon age 30	F	F	F	No
S92	22	46,XX	Cloacal malformation[g]	15	3.5 rigid	4	2	M	None	M	M→F (age 20)	F	Self-initiated gender change.
S93	18	46,XX	GD [c]	10	3.2	6	4	M	Treatment in other clinic (unknown), in infancy and age 7	M	M	M	No
S94	19	46,XY	GD [c]	14	4.1	4	(3)	F	Gonadectomy age 14	F	F	M	Self-initiated gender change. Just started living as male.

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S95	19	46,XY	GD [c]	19	Normal clitoris	2	(6)	F	None	F	F	F	No
S96	19	46,XY /45,X	GD [c]	19	5.5	6	(3)	F	None	F	F	F	No
S97	19	46,XY	GD [c]	19	5	8	(3)	F	None	F	F→A	A	Started living as male about one year after the study.
S98	20	46,XidicY	GD [c]	20	6	4	(3)	F	None	F	F→A (age 13)	A	Started living as male about one year after the study (age 21).
S99	21	46,XY	GD [c]	14	6	5	(2)	F	None	F	F→ M (age 14)	M	Self-initiated gender change.
S100	21	46,XY	GD [c]	21	5	4	(3)	F	Chordectomy age 11	F	F→M (age 7)	M	Gender reassignment (parents)
S101	23	46,XY	GD [c]	23	Normal clitoris	1	(7)	F	None	F	F	F	No
S102	27	46,XY	GD [c]	27	5	4.5	(3)	F	None	F	F	F	No
S103	27	46,XY	GD [c]	26	2.5	3	(4)	M	None	M	M	M	No
S104	39	46,XY	GD [c]	39	1	5	(5)	F	None	F	F	F	No
S105	41	46,XY	GD [c]	41	3	6	(4)	M	None	F	F→M (age 16)	M	Doubt own gender identity aged 8. Self initiated gender change. Married.
S106	24	46,XY	CAIS	24	Normal clitoris	1	(6)	F	None	F	F	F	No
S107	18	46,XY	PAIS [d]	11	3	5	(3)	M	None	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S108	18	46,XY	PAIS [d]	15	6.3	7	(3)	M	Chordectomy age 15; urethroplasty age 16	M	M	M	No
S109	20	46,XY	PAIS [d]	16	3.7	9	(2)	M	Gynecomasty, chordectomy, hypospadia corrections age 14 and 15	M	M	M	No
S110	27	46,XY	PAIS [d]	27	4.5	6	(4)	F	None	F	F→M (age 24)	M	Self-initiated gender change. Relocation to other island and start living as male.
S111	31	46,XY	PAIS [d]	26	2.6	6	(3)	F	Gynecomasty, chordee correction age 24; Hypospadia correction age 26.	F	F → M (age 27)	M	Gender ambiguity at admission. Change gender with medical consultancy. Married; adopted a child.
S112	19	46,XY	AAD [e]	14	5.3	7	(2)	M	Chordectomy age 15; urethroplasty age 19.	M	M	M	No
S113	22	46,XY	AAD [e]	17	1.5	3	(3)	F	None	F	F→M (age 19)	M	Self-initiated gender change.
S114	26	46,XY	AAD [e]	23	5.9	5	(3)	F	Gynecomasty, chordectomy, hypospadia correction age 23.	F	F→ M (age 24)	M	Gender ambiguity at admission. Change gender after medical consultancy. Married.
S115	20	46,XY	Undermas-culinization e.c.i.[f]	15	6	11	(2)	M	Hypospadia correction age 5.	M	M	M	No

(continued)

Table 6 Characteristics of patients with DSD: diagnoses, reported treatment received, and gender development history (n = 118) *(continued)*

Patients code	Age at study	Karyotype	Diagnoses [a-g]	Degree of masculinization at admission					Treatment received prior to study	Gender development history			
				Age	Phallus [h]	EMS [i]	Prader (or Quigley) [j]	Gender		At birth	Rearing	At study	Gender change [k]
S116	20	46,XY	Undermas-culinization e.c.i.[f]	15	6.5	9	(3)	M	Penis bend (twice), hypospadia corrections age 13, 15, 16.	M	M	M	No
S117	23	46,XY	Undermas-culinization e.c.i.[f]	23	6	9	(2-3)	M	None	F	F→M (age 17)	M	Self-initiated gender change. Relocate to other province and start living as male.
S118	28	46,XY	Undermas-culinization e.c.i.[f]	28	6	9	(2-3)	M	Chordectomy age 22 (other clinic).	F	F→M (age 17)	M	Self-initiated gender change.

Note. Age in years. EMS = external masculinization score; M = male; F = female; A = ambiguous gender identity; F→M = female-to-male gender change; M→F = male-to-female gender change; e.c.i. = e causa ignota (of unknown origin).

[a] CAH-SV refers to congenital adrenal hyperplasia with simple virilization type. CYP 21 mutation was confirmed in all patients (Juniarto, 2013).

[b] Mosaic sex chromosomal DSD.

[c] GD refers to gonadal dysgenesis, a condition in which subjects had abnormal hormonal testicular function with uni/bilaterally undescended testes. Androgen action was presumed to be fully effective. The clinical and biochemical presentation suggest gonadal dysfunction. Serum levels of luteinizing hormone and follicle stimulating hormone were elevated but testosterone, anti-müllerian hormone, and Inhibin are low for age, and no or diminished serum testosterone response to HCG.

[d] CAIS / PAIS = Complete / Partial Androgen Insensitivity Syndrome. A mutation in the AR gene was confirmed (Juniarto, 2013).

[e] AAD refers to 46,XY DSD and Androgen Action Disorder. All subjects had under-virilization (EMS < 9) and normal hormonal testicular function with uni/bilaterally undescended testes. We presume, in these patients, androgen actions not to be fully effective. The clinical and biochemical presentation were close to those of subjects with a mutation in the androgen receptor with elevated serum levels of luteinizing hormone, levels of testosterone, and anti-müllerian hormone but a mutation in the androgen receptor but a mutation in the androgen receptor could not be confirmed despite extensive analysis (Juniarto, 2013).

[f] Undermasculinization e.c.i. refers to 46,XY DSD male undermasculinization (EMS > 9) with unknown cause could be identified despite extensive analyses. Serum hormone values and response to HCG were all normal for age.

[g] Cloacal exstrophy.

[h] in centimetre (cm).

[i] Degree of masculinization based on external genital features, ranged from 0-12.

[j] Degree of genital masculinization. Prader stage is applied in 46,XX individuals, ranged from 0 (normal female) to 6 (normal male). Quigley stage is applied in 46,XY individuals, ranged from 1 (normal masculinization) to 7 (female phenotype).

[k] The term 'gender assignment' was applied for the first assigned official gender (usually registration in the birth file). The term 'gender reassignment' was applied for a gender change that had been the initiative of the parents or doctor. The term social gender role change was applied for patient initiative.

Matched controls. This group comprised 118 healthy adults matched for age, gender, and residential settings (rural, suburban, or urban). Initially, we preferred healthy siblings as matched control subjects as they share both potential genetic and social backgrounds with their affected brother or sister. However, this was not feasible due to difficulties in fulfilling the matching criteria (gender and age) within families as well as parental disapproval to involve healthy siblings in the study. Subsequently, we decided to compile a control group that consisted of healthy subjects matched to the above-mentioned criteria. The researcher visited the residential area of patients and established contact with a local leader (*Pak Lurah* or *Pak RT*) or midwife to find parents with a healthy child or adolescent or healthy adults who matched the criteria to be included as a control subject. After a potential matched control subject was identified, an invitation to join the study was given. The matched control subjects were informed about the study but only learned that they were selected to participate in a study on gender development carried out by the Psychology Faculty of the Diponegoro University in Semarang. It was chosen to do so in order to protect patients from being identified by their matched controls. Control subjects and/or parents of control subjects younger than 18 who liked to volunteer gave their written consent prior to assessment.

By design, the patients and the matched control subjects were comparable with respect to socio-demographic and cultural variables. Table 7 summarized the background of participants in this study. The majority of participants was males, lived in rural areas, and came from the Central Java province, was Javanese, and Moslem. The parents' educational background was varied from illiterate to university level with the majority having attended high school. Most parents worked in the low-income sector or were unemployed, particularly parents of patients with DSD.

Table 7 Socio-economic and cultural background of study participants

Characteristics background	Patients with DSD (*n*=118)	Matched Controls (*n*=118)	*p*
Age of study	13.8 ± 7.4	14.2 ± 7.1	.69
Region			
Central Java province	100 (84.7)	108 (91.5)	.12
Other provinces in Java	12 (10.2)	9 (7.6)	
Outside Java island	6 (5.1)	1 (.8)	
Ethnicity			
Javanese	108 (91.5)	106 (89.8)	.82
Non Javanese	10 (8.5)	12 (10.2)	
Religion			
Islam	112 (94.9)	108 (91.5)	.44
Non Islam	6 (5.1)	10 (8.5)	
Education – Father*	*n* = 116	*n* = 114	
Illiterate	18 (15.5)	15 (13.2)	.62
Elementary school	38 (32.8)	31 (27.2)	
High school	49 (42.2)	58 (50.9)	
University education	11 (9.5)	10 (8.8)	
Education – Mother*	*n* = 116	*n* = 117	
Illiterate	22 (19.0)	14 (12.0)	.33
Elementary school	38 (32.8)	34 (29.1)	
High school	48 (41.4)	58 (49.6)	
University education	8 (6.9)	11 (9.4)	
Occupation – Father*	*n* = 116	*n* = 114	
Unemployed	6 (5.2)	5 (4.4)	.06
Labor	64 (55.2)	46 (40.4)	
Self-employed	19 (16.4)	34 (29.8)	
Staff / Office job	27 (23.3)	29 (25.4)	
Occupation – Mother*	*n* = 116	*n* = 117	
Unemployed	57 (49.1)	39 (33.3)	.02
Labor	32 (27.6)	35 (29.9)	
Self-employed	12 (10.3)	28 (23.9)	
Staff / Office job	15 (12.9)	15 (12.8)	

Note. Data presented in *n* (%).The Fisher's exact test was applied; significant at $p < .05$
* indicates differences in *n*.

Procedures

This psychological study was part of the medical study evaluating the clinical diagnoses of patients with DSD that was started at 2004. The psychological follow-up was carried out between March 2007 to May 2011 and involved patients with DSD who had been referred to the DSD team from the Faculty of Medicine Diponegoro University and Dr Kariadi Hospital in

Semarang, Indonesia since 2004. The DSD diagnosis was based on the physical examination, results of cytogenetic analysis, hormonal data, and molecular analysis for gene mutations. The diagnostic procedures leading to the diagnosis of DSD have been described by Juniarto et al. (2012). Patients were invited to participate in the study and were given oral and written study information by a medical doctor (AZJ). After patients had given written consent, an appointment was made for the psychological assessment. The assessment was conducted by a clinical psychologist (AE) in the hospital or at home. She received training to deliver these measures and to conduct interviews with patients with DSD. In addition to the measures applied, the history of gender development was also obtained during the interview.

Measures

See study 1 for detailed description about measures applied in this study.

Statistical Analysis

Outcome measures were compared between patients and healthy controls, between patients and healthy controls stratified for gender, and between males and females stratified for patient/control participant group. Differences in continuous data with skewed distributions between two groups were summarized as medians (*Mdn*) and tested with the Mann-Whitney U test. Differences in categorical data between groups were compared using Fisher's Exact test. Differences between groups were considered significant at $p<.05$ (two sided). Due to the small number of cases in subgroups, comparisons of different subgroups of DSD diagnoses, or between patients who had changed their gender and patients who did not, or between treated and untreated groups of patients were avoided. As descriptive analysis we display individual data in scatter plots

Results

Social gender role change

Twenty-one patients had changed their social gender role. In four patients, the parents or health workers had initiated the gender reassignment when the patients were between two and eight years old. There were three patients with 46,XX karyotype and CAH-SV who were assigned as female at birth who but never had received glucocorticoid treatment. They had changed their

gender gradually at ages 2-3; the parents could not change their progressive masculinization as displayed through gender role behavior, preferences, and their self-identification as males. The remaining 14 patients took initiatives to change their social gender role between ages of 15 to 27.

The percentage of gender change was: 4 out of 60 children (6.7%); 2 out of 24 adolescents (8.3%); and 15 out of 34 adults (44.1%). Except for one patient with 46,XX and cloacal exstrophy who underwent a male-to-female gender role change, the remaining 20 patients underwent a female-to-male gender role change. Four patients underwent a social gender role change in about one year after this study whereas 17 patients had been living in their changed gender for 2-25 years prior to study. The majority of patients who had undergone a social gender role change sought medical help at our hospital during adolescence (five patients) or in adulthood (10 patients).

The social gender role change occurred in patients with a range of different karyotypes and DSD diagnoses, largely in patients with 46,XY karyotype and undermasculinization (17 out of 21 patients; 81%) but also in patients with 46,XX karyotype (4 out of 21 patients; 19%). Of 21 patients who changed gender, 16 (76.2%) had not received any treatment for their DSD conditions prior the study whereas five patients (23.8%) had undergone some genital surgery prior this study (Table 6).

All 21 patients disclosed their DSD conditions to their parents and/or spouses and received emotional support and acceptance for their DSD condition and their social gender role change. Only two patients had undergone a legal procedure to change their gender on their birth certificates.

Gender identity interview in children (GIIC)

Children with DSD raised as girls reported greater gender confusion than children with DSD raised as boys ($Mdn_G = 0$; $Mdn_B = 0$; $p = .004$). In the matched control groups the differences in gender confusion between girls and boys were not significant ($Mdn_G = 0$ *vs* $Mdn_B = 0$; $p = .54$). Comparison between the DSD and the matched control groups revealed that the gender confusion reported by the 42 children with DSD raised as boys and the 42 matched controls boys ($Mdn_P = 0$ *vs* $Mdn_C = 0$; $p = .44$) did not differ significantly. However, there is a tendency towards significance that children with DSD raised as girls reported greater gender confusion than the matched control girls ($Mdn_P = 0$ *vs* $Mdn_C = 0$; $p = .08$). As a scatter plot shows, individual differences in GIIC scores between

and within groups are present despite the equality of the median values (Figure 1). Of 18 girls with DSD, 15 girls had 46,XX karyotypes and CAH-SV. Of 60 children with DSD, four had undergone a gender reassignment (S01, S27, S34, S40; Table 6). All four scores higher on the GIIC than youngsters who had not experienced such a gender role change.

Gender Identity Questionnaire for Children (GIQC)

Parents of girls with DSD reported more cross-gender role behavior in their offspring than parents of matched control girls did (Mdn_P = 21.5 *vs* Mdn_C = 25.5, p = .047). No significant differences were found between parents' reports on boys with DSD and those for control boys (Mdn_P = 31.0 *vs* Mdn_C = 31.0, p = .27). In the DSD group, cross-gender behavior was reported more frequently by parents of girls than parents of boys (Mdn_G = 21.5 *vs* Mdn_B = 31.0, $p < .001$). Similarly, among matched controls, parents of girls reported more cross-gender role behavior than parents of boys (Mdn_G = 25.5 *vs* Mdn_B = 31.0, $p < .001$). In other words, parents of girls reported both feminine and masculine behaviors in their daughters, whereas parents of boys only reported masculine behavior in their sons, as demonstrated by a box plot (Figure 2a).

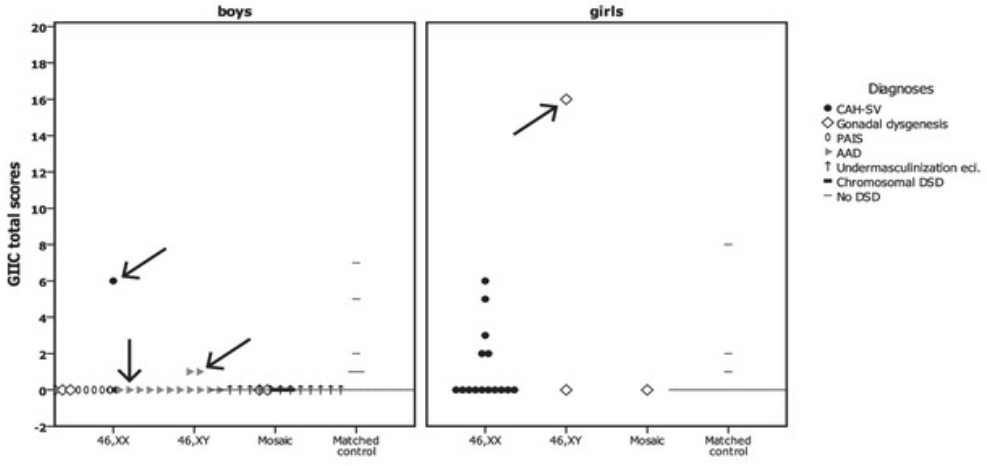


Figure 1 Gender identity confusion across groups and DSD diagnoses (data from the GIIC)
The plots showing individual data (total scores) of the Indonesian version of the GIIC across groups and DSD diagnoses
Score range: 0-18. 0 indicates no gender confusion. The higher scores indicate greater gender confusion.
The arrows point to four children with a history of gender change (S01, S27, S34, S40; Table 6).

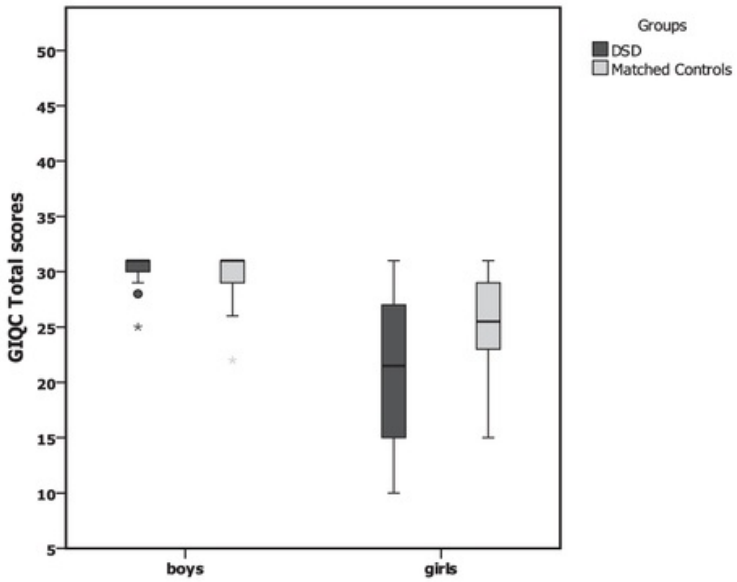


Figure 2.a Parental reports on children's gender role behavior (GIQC data)

Girls with DSD displayed more cross-gender behavior than the matched controls girls, whereas no significant differences were found among boys. Girls in both groups displayed more cross-gender behavior than the boys did.

A scatter plot (Figure 2b) shows the individual total scores of the GIQC across groups and diagnoses. Among girls with DSD, less gender role behaviors were reported by parents of girls with 46,XX karyotype and CAH-SV. In addition to these findings, 11 out of 15 girls with 46,XX karyotype and CAH-SV had received genital surgery and/or hydrocortisone medication in the 2-8 years prior to the study. There were three boys who had changed their social gender role (S01, S34, S40; Table 6) 2-4 years prior to this study. Finally there was one girl with 46,XY karyotype and gonadal dysgenesis who changed her social gender role into male after she had taken part in this study (S27; Table 6); she obtained lowest scores on the GIQC. Due to small number of cases, we could not perform further comparison analysis to support this finding statistically.

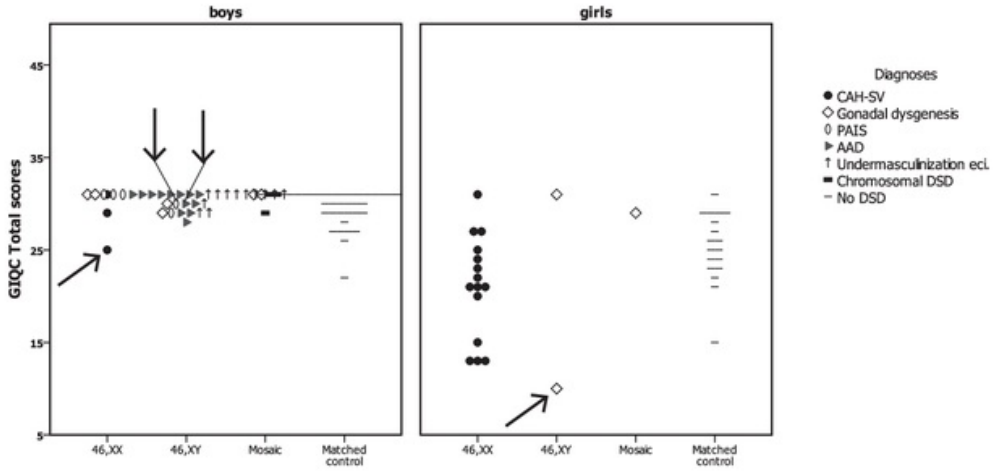


Figure 2.b The individual total scores on the Indonesian version of the GIQC across groups and diagnoses.

Scatter plots showing the individual total scores on the Indonesian version of the GIQC across groups and DSD diagnoses.
Possible score range: 5-50. Lower scores indicate less sex-typical gender role behavior in children that were reported by their parents.
The arrows pointed to four children with a history of gender change (S01, S27, S34, S40; Table 6).

Gender Questionnaire (GQ)

Adolescent girls with DSD reported significantly less sex-typical gender identity and gender role behavior during their lifetime and in the past 12 months than adolescent boys with DSD, during their lifetime and in the past 12 months ($Mdn_G = 2$ *vs* $Mdn_B = 2$; $p = .02$; $Mdn_G = 2$ *vs* $Mdn_B = 2$; $p = .01$, respectively). They also reported more cross-gender identity and more cross-gender role behavior during lifetime and in the past 12 months than adolescent boys with DSD ($Mdn_G = 5$ *vs* $Mdn_B = 5$; $p = .04$; $Mdn_G = 5$ *vs* $Mdn_B = 5$; $p = .01$, respectively).

Adults men with DSD scored higher on the lifetime but not on the past-12 months scales of the gender questionnaire, reflecting they evaluated themselves being less sex-typical in identity and behavior and had faced more problems with respect to their gender identity and behavior (gender identity and gender role behavior: $Mdn_P = 2.5$ *vs* $Mdn_C = 2$; $p = .01$; cross-gender identity and behavior: $Mdn_P = 6.5$ vs $Mdn_C = 5$; $p = .01$). The majority (14 of 19; 73.7%) of men with DSD had initially been raised as girls but had changed their social gender role to be men later in life. In contrasts, women with DSD did not differ significantly from the control women in their gender identity and gender role behavior during lifetime and in the past 12 months ($Mdn_P = 2$ *vs* $Mdn_C = 2$; $p = .77$; $Mdn_P = 2$ *vs* $Mdn_C = 2$; $p = .77$, respectively) nor in cross-gender identity and

behavior during lifetime and past 12 months ($Mdn_P = 5$ *vs* $Mdn_C = 5$; $p = .24$; $Mdn_P = 5$; $Mdn_C = 5$; $p = .72$, respectively).

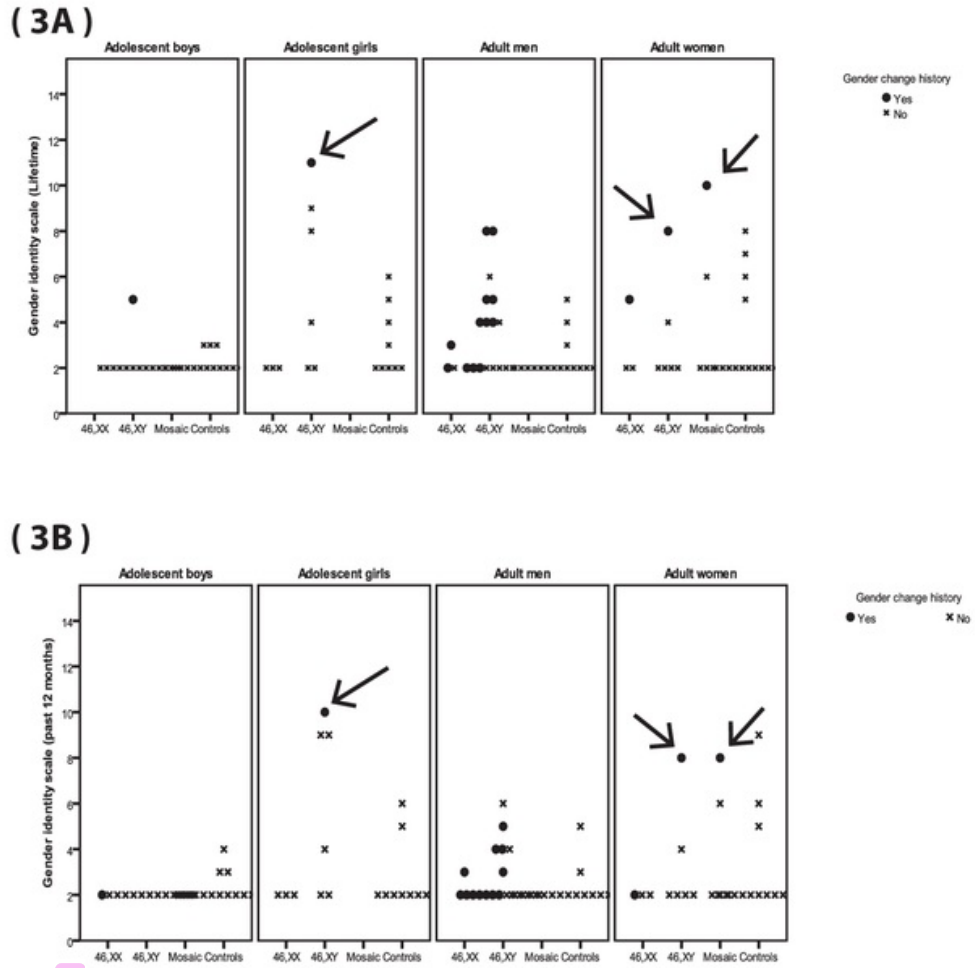
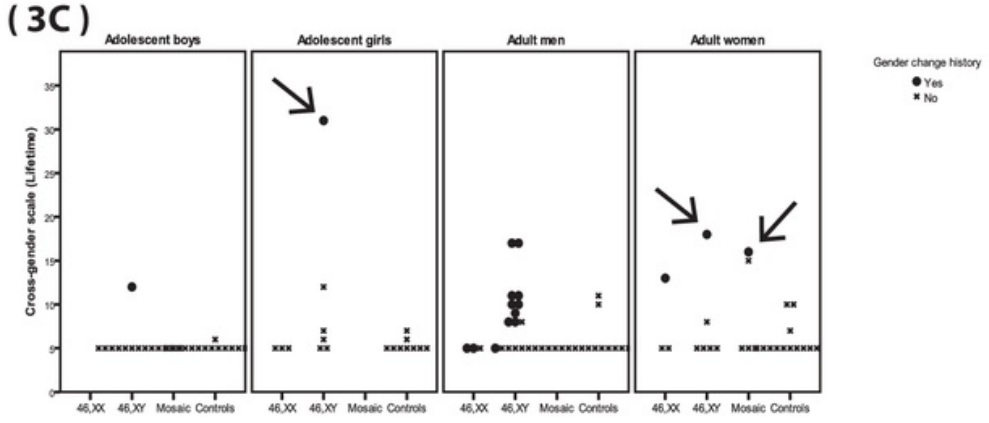


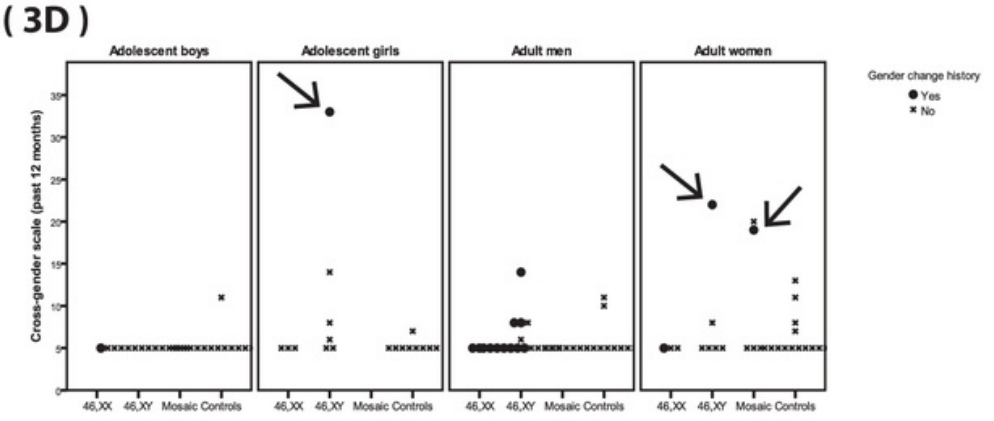
Fig. 3 Gender identity and gender role behavior in patients with different karyotype and gender change history (GQ data)

These plots (3a, 3b) display individual scale score on the gender identity and behavior reported during lifetime (Fig. 3a) and in the past 12 months (Fig. 3b). Possible scale score range: 2-14. Higher scores indicate less sex-typical gender identity and behavior reported during lifetime or in the past 12 months. The arrows indicate patients who changed gender post study (S80, S97, S98; Table 6).

Of 24 adolescents and 34 adults with DSD who responded to questions in the GQ, there are two adolescents and 15 adults who had a history of gender change. Figure 3a-d depicts the individual total scores of GQ among patients with and without a history of gender change. Of 21 patients who had a history of gender change, there are three patients (S80, S97, S98) who were in the start of the process to change their social gender role and who therefore had been,

assessed with a questionnaire for female, obtained high score on all GQ scales; both measures on gender during lifetime and in the past 12 months (see patients indicated by arrows in the Figure 3). This is in contrast to the majority of patients who had been living in their changed social gender role prior to study: these men scored high on the lifetime-scales but scored low on the past 12 months-scales.





These plots (3c, 3d) display individual scale score on the cross-gender identity and behavior reported during lifetime (3c) and in the past 12 months (3d). Possible scale score range: 5-35. Higher scores indicate more cross-gender identity and behavior reported during lifetime or in the past 12 months.
The arrows indicate patients who changed gender post study (S80, S97, S98; Table 6).

We compared patients who had received surgical and hormonal treatment with patients who had not received treatment but did not find significant differences in all scales of the GQ (Figure 4).

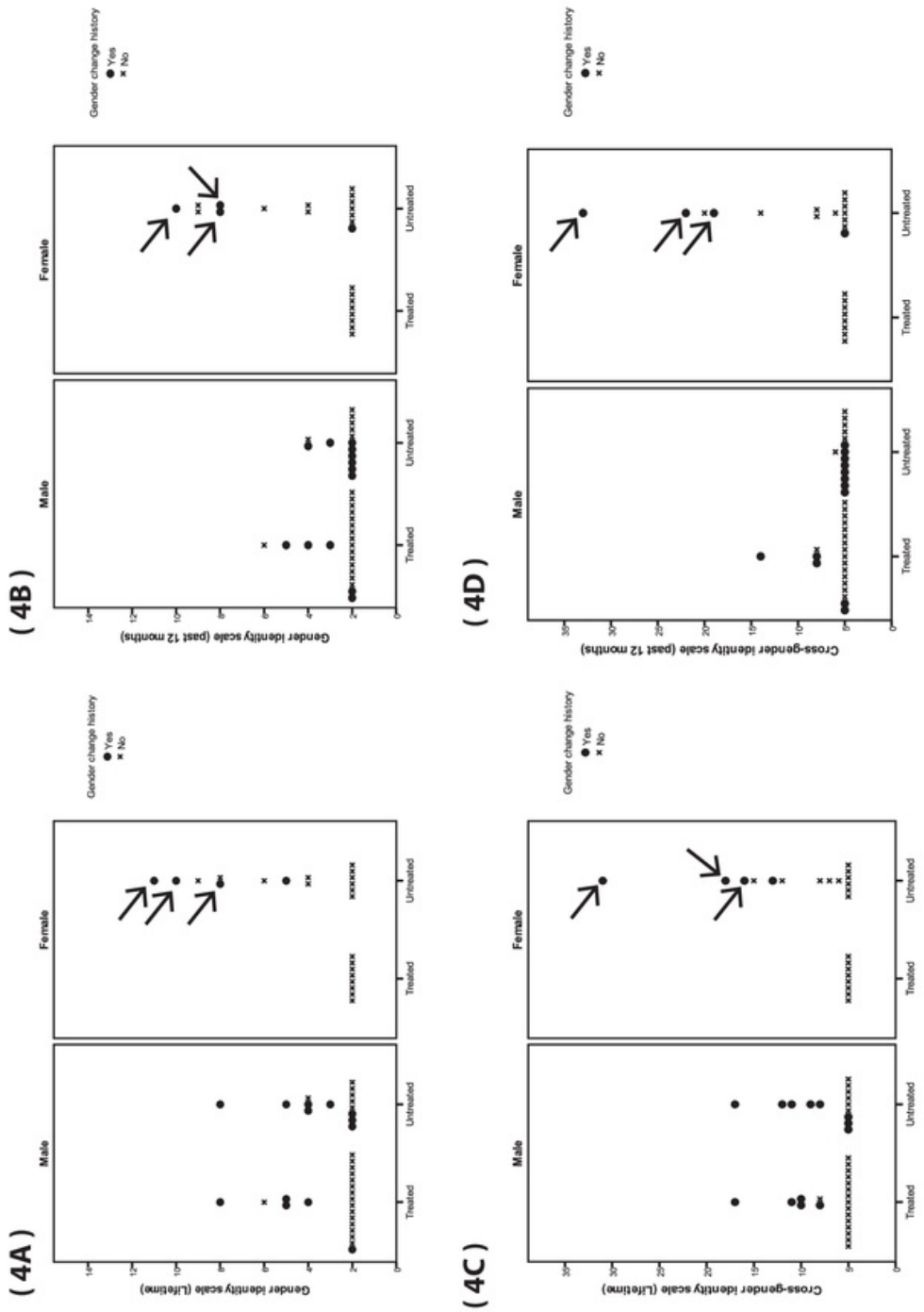

(4A)
Male
Female
Gender change history
Yes
No
Gender identity scale (Lifetime)
Treated
Untreated
(4B)
Male
Female
Gender change history
Yes
No
Gender identity scale (past 12 months)
Treated
Untreated
(4C)
Male
Female
Gender change history
Yes
No
Cross-gender identity scale (Lifetime)
Treated
Untreated
(4D)
Male
Female
Gender change history
Yes
No
Cross-gender identity scale (past 12 months)
Treated
Untreated

Fig. 4 Comparison on GQ data between treated and untreated adolescents and adult patients

Notes. The plots (4a, 4b) display individual total scores of adolescents and adult patients in the gender identity and gender role behavior reported during lifetime (fig. 4a) and in the past 12 months (fig. 4b). Possible total score range: 2-14. Higher scores indicate less sex-typical gender identity and behavior reported during lifetime or in the past 12 months. Comparison analysis revealed significant differences in females, but not in males, in all scales of GQ. Adolescents girls and adult women with DSD who never had received medical treatment reported less feminine gender-identity and gender role behavior than adolescent girls and adult women with DSD who had received some treatment, during lifetime and in the past 12 months.

The plots (4c, 4d) display individual total scores of treated and untreated adolescents and adult patients, males and females, in the cross-gender identity and cross-gender role behavior reported during lifetime (fig. 4c) and in the past 12 months (fig. 4d). Possible total score range: 5-35. Higher scores indicate more cross-gender identity and cross-gender role behavior reported during lifetime or in the past 12 months. Comparison analysis revealed that adolescents girls and adult women with DSD who never had received medical treatment more frequently reported cross-gender identity and masculine gender role behavior than adolescent girls and adult women with DSD who had received some treatment, during lifetime and in the past 12 months. The arrows indicate patients who changed their gender post study (S80, S97, S98; Table 6).

Activities Questionnaire (AQ)

Figure 5 demonstrated the findings on the Activities Questionnaire. Adolescent boys and girls, in either the DSD or the matched control group, recalled different preferences in childhood activity. Among adolescents with DSD, boys recalled more masculine activities than girls did ($Mdn_B = 20$ *vs* $Mdn_G = 16.5$; $p < .001$), whereas girls recalled more feminine activities than boys did ($Mdn_G = 10$ *vs* $Mdn_B = 5$; $p = .002$). Similar findings were reported among the matched control adolescents: boys recalled more masculine activity than girls did ($Mdn_B = 19$ *vs* $Mdn_G = 14.5$; $p = .008$), and girls recalled more feminine activity than boys did ($Mdn_G = 14.2$ *vs* $Mdn_B = 5$; $p = .001$).

Adolescent girls with DSD did not differ from the matched control girls in recalled masculine and feminine activities in childhood ($Mdn_P = 16.5$ *vs* $Mdn_C = 14.5$; $p = .82$ and $Mdn_P = 10$ *vs* $Mdn_C = 14.2$; $p = .42$, respectively). Similarly, adolescent boys with DSD did not differ from the matched control boys in recalled masculine and feminine activities in childhood ($Mdn_P = 20$ *vs* $Mdn_C = 19$; $p = .42$ and $Mdn_P = 5$ *vs* $Mdn_C = 5$; $p = .99$, respectively).

Men and women in both the DSD and matched control groups, recalled differences in the childhood activities they preferred. Among adults with DSD and matched controls, men recalled more masculine activities than women did ($Mdn_M = 18$ *vs* $Mdn_W = 14.5$; $p < .001$ and $Mdn_M = 19$ *vs* $Mdn_W = 13$; $p = <.001$, respectively) whereas women recalled more feminine activities than men did ($Mdn_W = 11.7$ *vs* $Mdn_M = 5.0$; $p < .001$ and $Mdn_W = 13.4$ *vs* $Mdn_M = 5.0$; $p < .001$, respectively). Women with DSD did not differ from the matched control women in recalled masculine and feminine type of childhood activities ($Mdn_P = 14.5$ *vs* $Mdn_C = 13$; $p = .45$ and $Mdn_P = 11.7$ *vs* $Mdn_C = 13.4$; $p = .50$, respectively). Men with DSD do not differ from the matched control men in recalled masculine and feminine type of childhood activities ($Mdn_P = 18$ *vs* $Mdn_C = 19$; $p = .76$ and $Mdn_P = 5$ *vs* $Mdn_C = 5$; $p = .37$, respectively).

Figure 5 Adolescent and adult reports on their preference for (a) masculine and (b) feminine type of childhood activities (data from the Activities Questionnaire). The plots show that patients with DSD, either male or female, did not differ from the matched controls in their preferences for childhood activities. Either in adolescent or adult group, males recalled more masculine type of childhood activities than females; females recalled more feminine activities than males. Females preferred both masculine and feminine type of activities; whereas males preferred masculine activities only.

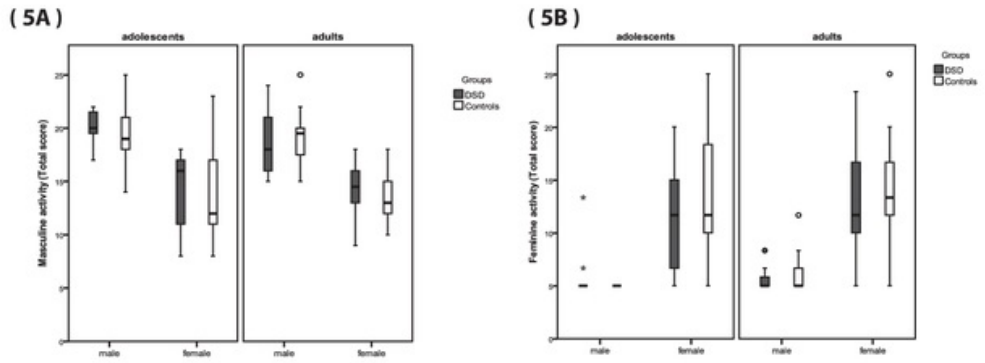


Figure 5 Adolescent and adult reports on their preference for (a) masculine and (b) feminine type of childhood activities (data from the Activities Questionnaire). The plots show that patients with DSD, either male or female, did not differ from the matched controls in their preferences for childhood activities. Either in adolescent or adult group, males recalled more masculine type of childhood activities than females; females recalled more feminine activities than males. Females preferred both masculine and feminine type of activities; whereas males preferred masculine activities only.

Discussion

This study aimed to investigate the gender development of Indonesian patients with DSD who, for many years, had been left without a diagnostic workup and treatment or only received limited treatment. During their initial visit for medical help, questions on gender assignment, reassignment, and change of social gender role were often addressed. As studies in non-Western populations are limited, we conducted this study and assessed the gender identity and gender role behavior of Indonesian patients with DSD whom only recently diagnostic workup and treatment became available. No such study has been performed before in Indonesia and no locally validated instruments were available. Hence, we decided to conduct an explorative study and apply Indonesian translations of measures applied in comparable studies in Western countries. We were well aware that application of Western measures in non-Western populations may lead to various types of methodological problems but we have taken all possible effort to minimize these problems prior to implementation so that we could reach our goal: gaining insight in gender development of Indonesian children, adolescents, and adults with DSD. To our knowledge, this is the first study reporting gender development in patients with DSD in Indonesia and also the first study in this fields that combines a psychological evaluation alongside clinical management. We are aware of Graham's studies on intersexuality among *Bissu,* the Bugis priests (Graham, 2009), but her anthropological observations on this cultural

phenomenon are not applicable for individuals with DSD who have to deal with their condition in daily life.

Social gender role change

Most studies on social gender role change during puberty report on patients diagnosed with 5α-reductase 2 and 17β-hydroxy-steroid dehydrogenase 3 deficiencies. Patients born with a disorder in the biosynthesis of testosterone are severely undermasculinized at birth. They had been assigned females at birth and had been diagnosed in puberty when they started to masculinize and sought medical help (Cohen-Kettenis, 2005; Costa, Domenice, Sircili, Inacio, & Mendonca, 2012; Mendonca et al., 1996). Gender reassignment and social gender role change in children and adolescents with DSD had been reported in several countries, i.e. China (Jingde et al., 2009), India (Ammini et al., 2002; Gupta, Bhardwaj, Sharma, Ammini, & Gupta, 2010), USA (Reiner, 2005), and Egypt (Ismail & Mazen, 2010). But these studies were conducted in patients who had received treatment and detailed information on gender development were lacking. The percentage of a social gender role change among late diagnosed and untreated patients with DSD is hardly known. No such study has been conducted before as recent studies were mostly conducted among treated patients.

We observed that among late diagnosed and untreated patients with DSD there was a substantial number of patients (21 patients) who had undergone a gender reassignment or had changed their social gender role. The majority of these patients (81%) had 46, XY DSD and undermasculinization due to different causes. Only one patient, with 46,XX cloacal exstrophy, wished to change social gender from male to female. Most of these patients developed a wish to change their social gender role during puberty or adulthood (aged 15 or older). In three siblings (Table 6, patients S01, S86 and S87), a social gender role change happened gradually at an earlier stage in life (aged 2-3). These patients had 46,XX DSD due to CAH-SV, were assigned female at birth, and had never received glucocorticoid treatment. Left untreated, excessive levels of androgens masculinized the bodies and behavior of these children. The parents supported their daughters' wish to change gender.

The remaining twenty-one patients with 46,XX karyotype and CAH-SV did reported no problems in gender identity. Two of them were assigned male at birth, never received glucocorticoid, and were still living in the male gender. Nineteen patients were assigned female at birth, received glucocorticoid

treatment following genital surgery and were living in the assigned female gender. This study highlighted the importance of early diagnosis, regular glucocorticoid treatment and genital corrections to minimize the risk to develop problems in gender identity in females with CAH. In many patients, gender had been assigned by the parents, midwives, or other medical health workers without the help of any diagnostic evaluation. We do not know which criteria had been used in the decision to raise the neonate as a boy or a girl. Regardless of diagnoses, we assume that gender assignment had been done based on genital phenotype and/or parental wishes. Further stratified comparison analysis between patients with different DSD diagnoses raised in different gender could not be done due to the small number of cases. A follow-up study on our patients who reported social gender role change is needed to investigate whether the gender acquired later in life will be stable and will prevent gender dysphoria later in life. Our findings are in accordance with findings in patients with disorders in the biosynthesis of testosterone published by Imperato-McGinley, Peterson, Gautier, & Sturka (1979), Rösler, Silberstein, & Abeliovich (1996), Mendonca (1996) and Melo et al (2003). We assume that in our patients with 46,XY DSD and hypovirilisation at birth, the masculinization process in puberty gave an impulse for male gender identity development and consequently, for a wish to change the social gender role (Sisk and Zehr, 2005). Here it is difficult to discern biological and social influences. In puberty, androgens change the body and the brain (Crone & Dahl, 2012). The development of a male identity may be a direct effect of the action androgens exert in brain areas related to one's gender identity, if such brain areas exist. On the other hand, the perceived changes of the body, which are contrary to the expected pubertal body changes, may introduce gender confusion. In daily life, these body changes will make it difficult to present oneself in the assigned gender. The person may be mistaken for a member of the opposite sex, or may become aware of the embarrassment displayed by strangers who, on seeing someone with an ambiguous body, are confused about how to address the patient. On many occasions, patients were misidentified as transsexuals and nicknamed *Waria* or *Banci*. Treatments to reverse established changes of masculinization are often expensive for poor people to consider. For these individuals, there may be social and economic advantages to continuing life as men.

This study demonstrates that many, but not all, adults with DSD in Indonesia experienced long-term gender identity problems, particularly those patients whose behavior and interests were not in line with the assigned gender and who developed ambiguous bodies. Our finding confirms the idea that diagnostic evaluation soon after identification of DSD is essential, not only to provide necessary medical care, but also to help parents and patients in social adjustment and coping with the condition. It is striking that changes in social gender role is particularly seen among patients living in poverty or in regions in which medical knowledge and help are limited. From table 6 it can be inferred that in a substantial number of patients, gender-related problems had been long lasting before the patients took the decision to change gender. Many of them made this decision by themselves without medical and psychological counseling. Early diagnostic evaluation, proper treatment, education on the DSD condition and its consequences on body and gender development may reduce the burden to live in ambiguity. Such understanding would make it easier to accept the conditions and its psychological consequences. It is urgent for the patients and parents to be identified quickly and referred to a specialized center where education about DSD and genetic as well as psychological counseling are available. For this purpose, raising awareness and involvement among health practitioners in the primary care centers, as well as other health providers, is essential.

Gender identity and gender role behavior in children

On the measures for gender identity and gender role behavior, children with DSD raised as girls experienced greater gender confusion than the matched control girls or children with DSD raised as boys. The parents of girls with DSD reported more masculine behavior in their daughters than parents of the matched control girls did. The majority of these girls had 46,XX karyotype and CAH. Our findings are in line with previous studies conducted in Western countries that reported masculine behavior in girls with 46,XX karyotype and CAH (Berenbaum et al., 1999, 2000; Collaer & Hines, 1995; Zucker et al., 1993) and with studies comparing Western children with a gender identity disorder to healthy controls (Johnson et al., 2004). Girls showed a wider range of preferred activities and play behavior than boys, whereas boys seemed to narrow their focus on sex-typical activities and gender role behavior. It has been assumed that, with respect to cross gender role behaviors, Western societies are more

tolerant towards girls; they have more freedom to choose toys and games they like. In contrast, boys who display feminine behaviors and interests will receive more critics, ridicule, and social pressure to conform on typical male behaviors and interests (Golombok & Fivush, 1994).

Gender identity and gender role behavior in adolescents

Data from adolescents revealed that girls with DSD reported more dissatisfaction with the assigned gender and had higher scores on cross-gender identity/behavior than boys with DSD. These differences were not observed among matched control boys and girls. Moreover, adolescents with DSD and the matched controls reported similarities in recalled childhood activities. Boys predominantly preferred masculine activities only, whereas girls recalled both masculine and feminine activities.

Physical and psychological changes during puberty make the adolescent more aware about their gender identity, their sex, and the social implication of their sex. On top of this, the adolescents with DSD should be informed in more details about their own condition to facilitate better understanding about their DSD condition. Adolescents with DSD have to deal with these new perspectives and find ways to integrate these in their identities. This process may cause confusion on gender identity and social adjustment. Our data suggested that puberty is the critical period to develop problems related to gender identity as indicated by the majority of patients that undergone social gender role change during adolescence or adulthood. Therefore, psychological counseling and patient education should be offered to facilitate coping with DSD and its consequences in adulthood.

Gender identity and gender role behavior in adults

Data from the Gender questionnaire indicate that adults with DSD living as men at the time of study reported more dissatisfaction with the assigned gender, more often identified oneself in the opposite gender, and more often displayed cross-gender behavior during lifetime than the matched control men. These differences, however, were not reported in relation to the period of the past 12 months. It is important to remember that the majority of men with DSD in this study had undergone a female-to-male gender change and had been living as male within 2-25 years before this study. Thus, they reported their dissatisfaction, experiences, and gender-related problems while living as

women (as measured period of lifetime), and their satisfaction and experiences while living as men (as measured in the past 12 months).

The Activities Questionnaire could distinguish well between typically male and female childhood activities. Comparison between patients and matched controls revealed no differences in recalled feminine or masculine type of childhood activities. Our findings were similar to a previous study conducted in a Western country (Hines et al., 2003), although our study comprised many patients with a history of gender change whereas Hines' study included no such patients. Those patients who had been living as men for more than two years prior to joining the study reported similar scores on masculine gender identity and gender role behavior to the matched controls. It suggests that they adjusted well to their new social gender role as men. According to figures of prevalence, no gender identity problems were reported among matched controls subjects (Cohen-Kettenis & Gooren, 1999).

Treated and untreated groups of comparison

There has been a debate whether early treatment of ambiguous genitalia will prevent gender problems later in life. In Western countries, treatment for DSD -such as surgical correction of the genitalia and hormonal treatment- is usually offered early following identification; therefore studies among untreated patients in Western countries are lacking. In Indonesia, diagnosis and treatment are not always available. Among patients who received treatment, there was variety in treatment (hormonal or surgical), timing, availability (i.e. surgery series had not been completed due to financial reasons), compliance, and follow up of treatment. Moreover, no data on genital ambiguity at birth were recorded. Considering these limitations, we could not compare treated and untreated groups of patients to test the treatment effectiveness. Nevertheless, as many of these patients entered our hospital during adolescence or adulthood, we investigated differences in gender-related problems between treated and untreated patients and revealed no significant differences.

Study limitation

This study has several limitations. First, the small number of participants, particularly young girls and adolescents, often served as a barrier in a study on rare diseases like DSD. Small sample size prevented us from conducting subgroup or stratified comparisons with sufficient power. Instead, the

presentation of individual data in scatter plots can help us to interpret findings from highly skewed data distributions in small samples. Second, with respect to the utilization of Western measures, we learned that several questions from the Western measures need to be applied carefully and considered for application in non-Western cultures. Future improvement on these measures should include local concepts of femininity and masculinity, gender role behavior, and the social-cultural context of the study population. Third, the lack of uniformity in clinical management in these study groups, increased the heterogeneity of the study groups and, possibly, also contributed to heterogeneity in measurements. This limitation also inhibited us to compare treated and untreated groups of patients or investigate more specific research questions.

Conclusion

This study reported gender-related problem among late diagnosed patients with DSD in Indonesia, particularly among patients who have been raised as females. It also reported a large number of patients who underwent female-to-male gender reassignment or social gender role change, largely reported among adults but also found in adolescents and children with DSD. Many of these patients experienced great problems related to their gender identity development. The change of gender was of great help to reduce the gender problems. Such large percentages of patients with a wish for a social gender role change are not observed in countries and areas that offer diagnostic evaluation and treatment just after identification of an ambiguous genital or ambiguous body development. Therefore it is urgent for the affected individuals to be identified and referred to a specialized center that offer diagnostic evaluation, treatment, parent and patient education and genetic and psychological counseling. For countries that do not have these specialized centers or only can provide medical help to prosperous patients we strongly recommend: 1) to promote early referral and identify persons with DSD by educating health practitioners in the primary care centers; 2) to promote parent and patient education on DSD and its long-term consequences; 3) to perform an integrated clinical and psychological care pathway immediately following referral; 4) to promote long-term medical and psychological follow up; and 5) to conduct follow-up studies to evaluate diagnostic procedures and treatment.

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Chapter 5

Emotional and behavioral problems in Indonesian children, adolescents, and adults with disorders of sex development

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Abstract

Objective: To investigate emotional and behavioral problems among Indonesian patients with disorders of sex development (DSD) who received little or no medical treatment prior to this study. As a consequence of non-treatment, deviations in body development could be noticed easily

Method: We compared 118 Indonesian patients with DSD aged 6-41 years (60 children, 24 adolescents, 34 adults) and 118 healthy control subjects matched for age, gender, and residential settings (rural, suburban, or urban area). We used the Child Behavioral Checklist (CBCL/6-18), Youth Self-Report (YSR), and Adult Self-Report (ASR) to assess emotional and behavioral problems. We examined differences on emotional and behavioral problems between patients and matched controls and between patients with different types of DSD. Patients who scored within the borderline range were also identified.

Results: Children and adults with DSD reported more emotional and behavioral problems than matched controls, but adolescents did not. Internalizing problems were often reported among adult patients and untreated patients. No significant differences in emotional and behavioral problems were found across different diagnostic groups. No significant difference were found between young girls with CAH and matched control girls in all CBCL scales, except in the Withdrawn scale.

Conclusions: Emotional and behavioral problems reported among patients with DSD who had been left untreated for long time showed some differences and similarities to studies reported in Western countries. Children and adults with DSD, particularly, were at risk of having emotional and behavioral problems. The reported emotional and behavioral problems were not associated with specific DSD diagnoses.

Keywords: emotional problem, behavioral problem, disorders of sex development (DSD), untreated, Indonesia

Background

Disorders of sex development (DSD) refers to a group of congenital conditions in which the development of chromosomal, gonadal, and anatomical sex is atypical (Hughes, Houk, Ahmed, & Lee, 2006). The atypical development of the anatomical sex starts prenatally and leads to the development of ambiguous internal and/or external genitalia, in puberty often followed by the development of ambiguous secondary sex characteristics. The large majority of patients are infertile. DSD is an umbrella term and there is a large variety in genotype and phenotype between the different DSD conditions. The combination of male and female sex characteristics combined with infertility gives patients with DSD a delicate position in society. In order to obtain citizenship, newborns have to be registered in governmental birth files. Most societies maintain a binary division in men and women, and infants with DSD usually will be assigned the male or female gender. DSD is a medical condition that needs medical attention soon after it has been identified. Diagnostic evaluation will reveal expected somatic and psychological development in the future and hence facilitates gender assignment (Hughes, et al., 2006). Medical treatments will prevent illness and corrections of genital ambiguity and avoidance of development of an ambiguous body in puberty may protect the patient from ostracism and ridiculization (Hughes, 2008).

DSD conditions are rare and many Indonesian health workers have limited knowledge. Often neonatal diagnostic procedures are not available. Indonesian parents who want to obtain citizenship for their child are forced to assign a gender without a diagnostic workout. The gender assigned in infancy, may not fit well later in life. So living with DSD, particularly when gender does not fit and being outcast, can be stressful for the affected person and the family members. Schützmann, Brinkmann, Schacht, and Richter-Appelt (2009) reviewed 11 studies on emotional and psychological problem among patients with DSD which showed inconclusive results, partly because lack of uniformity in measures used to assess emotional and behavioral problems in patients with DSD. These authors conducted a study on psychological distress, self-harming behavior, and suicidal tendencies in 37 adults with DSD and found that 59% of adults with DSD scored in the clinical range. Psychological distress was independent of the presence of ambiguous genitalia at birth or age of surgery, and patients with congenital adrenal hyperplasia (CAH) were less distressed

than patients with other types of DSD (Schützmann, et al., 2009). Kleinemeier, Jürgensen, Lux, Widenka, and Thyen (2010) conducted studies on adolescents with different types of DSD and concluded that DSD had no impact on the mental health of the youngsters. Recently Zhu and colleagues (2010) observed more emotional and behavioral problems in boys with DSD compared to their matched controls, whereas no significant differences between groups were found among girls. Studies carried out by Trautman, Meyer-Bahlburg, Postelnek, and New (1995) and Hirvikoski and colleagues (2008) did not reveal behavioral problems in girls with CAH whereas Oner and colleagues (2011) observed more externalizing behavior and general behavioral problems than in the control girls.

In Indonesia, as a consequence of late identification of DSD, diagnostic procedures are postponed or not performed, and many patients never receive any medical treatment for their DSD for most of their life. The Indonesian patients had to live with ambiguous genitalia, doubts about their gender and, from adolescence onwards, with bodies that have both male and female sex characteristics. Indonesia is an archipelago with a great diversity as it has about 300 ethnic groups and five recognized religions (WHO, 2006). Indonesia also categorized as a collective society in which people are expected to conform with social norms and ideals in the society (Hofstede, 2001). A binary sex is the only accepted sex category in Indonesia. We assumed that these ambiguities could put them at risk for developing emotional and behavioral problems. To our knowledge, no such study in late diagnosed and untreated patients with DSD has been reported before.

Our study aims to investigate emotional and behavioral reported among children, adolescents, and adult patients with DSD by addressing the following research questions:

a) Do children, adolescents, and adult patients with DSD experience more emotional and behavioral problems compared to the matched control subjects?

b) What types of emotional and behavioral problem are seen in these patients?

Method

Study design

In this study, we evaluated emotional and behavioral problems reported among Indonesian children, adolescents, and adult patients with a disorder of sex development (DSD) who had entered medical services late in life. The study protocol had been approved by the board of the ethical committee from Faculty of Medicine, Diponegoro University, Semarang, Indonesia.

Participants

Patients with DSD. This group comprised 118 patients diagnosed with DSD: 60 children (42 boys, 18 girls; aged 6-11), 24 adolescents (15 boys, nine girls; aged 12-17), and 34 adults (20 men, 14 women; aged 18-41). All patients had been born with a DSD condition, were age 6 or older and the majority only recently had become under medical attention. We excluded patients younger than 6 years old, patients with 46,XY and 46,XX DSD and features suggestive of a dysmorphic syndrome, patients with non-mosaic sex chromosome DSD and patients with DSD and intellectual disabilities (indicated from parent reports on their child's academic achievements and/or observed by the medical doctor in interaction with the patient). Of the 168 eligible patients, 21 patients (12.5%) were lost to follow-up due to relocation to other islands or invalid contact details, and 29 patients (17.3%) declined participation. Table 1 summarized the diagnostic characteristics of the 118 patients in the study. Of these118 patients, 61 patients (51.7%) had received some treatment, whereas 57 patients (48.3%) had not received any medical treatment prior to this study. Medical treatments comprised hormonal medication and genital surgery. Unlike in western countries, therapies in Indonesian patients often had been impeded. Main reasons for intermission were lack of finance for follow-up genital surgery or irregular availability of glucocorticoid medication. Eleven children with 46,XX CAH who were raised as girls had received hormonal treatment between two and eight years prior to this study.

Table 1 Clinical diagnosis of patients in the study

DSD diagnoses	Children	Adolescents	Adults	Total
46,XX CAH-SV [a]	18	2	4	24
Androgen insensitivity syndrome (AIS) [b]	5	5	6	16
Gonadal dysgenesis [c]	12	7	16	35
46, XX Cloacal exstrophy	-	1	1	2
Androgen action disorder (AAD) [d]	13	6	3	22
Under masculinization unknown cause [e]	12	3	4	19
Total	60	24	34	118

Note. CAH-SV = simple virilizing type of congenital adrenal hyperplasia

[a] CYP 21 mutation was confirmed (Juniarto et al., 2013).

[b] AR gene mutation was confirmed (Juniarto et al., 2013).

[c] A condition in which patients had abnormal hormonal testicular function with uni/bilaterally undescended testes. Androgen action was presumed to be fully effective. The clinical and biochemical presentation suggest gonadal dysfunction. Serum levels of luteinizing hormone and follicle stimulating hormone were elevated but testosterone, anti-müllerian hormone, and Inhibin are low for age, and no or diminished serum testosterone response to HCG. Including in this group is patients with chromosomal DSD.

[d] 46,XY DSD and disorder in androgen action. All subjects had undervirilization (EMS<9) and normal hormonal testicular function with uni/bilaterally undescended testes. We presume, in these patients, androgen actions not to be fully effective. The clinical and biochemical presentation were close to those of subjects with a mutation in the androgen receptor with elevated serum levels of luteinizing hormone, levels of testosterone, and anti-müllerian hormone but a mutation in the androgen receptor but a mutation in the androgen receptor could not be confirmed despite extensive analysis (Juniarto et al., 2013).

[e] Under masculinization unknown cause refers to 46,XY DSD male undermasculinization (EMS > 9) with unknown cause could be identified despite extensive analyses. Serum hormone values and response to HCG were all normal for age.

Matched controls. This group comprised 118 individuals: 60 children, 24 adolescents, and 34 adults. For each patient, a healthy subject matched for age, gender, and residential settings (rural, suburban, or urban area) was found. Control subjects were healthy, had been raised in the same gender as the matched patient, were about the same age and had been living in a similar residential settings (rural, suburban, or urban area), reflecting to be raised under similar socioeconomic conditions. Three siblings joined the study, the remaining matched control subjects were approached through the local leader (in *Bahasa: Pak RT* or *Pak Lurah*) or midwife. After a potential matched control subject was identified an invitation to join the study was given. In order to guarantee the privacy of the patients the *Pak RT, Pak Lurah,* or midwife and the matched control subjects were informed that this study was a population study on emotional and behavioral problems carried out at the Psychology Faculty of the Diponegoro University. None of the potential matched control subjects

declined participation in the study. After the control subjects gave their written consent to participate in the study, data collection was conducted following the similar procedure as the patients did.

Measures

Data on emotional and behavioral problems were obtained using ASEBA (Achenbach System of Empirically Based Assessment) scales: the Child Behavior Checklist (CBCL/6-18; Achenbach & Rescorla, 2001), the Youth Self-Report (YSR; Achenbach and Rescorla, 2001), and the Adult Self-Report (ASR; Achenbach & Rescorla, 2003). These ASEBA measures assess behavioral and emotional problems reported over the past six months. Each item is rated on a 3-point scale: 0 (not true), 1 (somewhat or sometimes true), and 2 (very true or often true). For most scores, higher scores indicate a higher level of emotional and behavior problems.

CBCL/6-18. The CBCL/6-18 is a 120-item standardized parent-report measure of behavior problems in children aged 6 to 18 years (Achenbach & Rescorla, 2001). It measures eight scales: Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought Problems, Attention Problems, Rule-Breaking Behavior, and Aggressive Behavior. This measure had been validated across 30 societies and had satisfactory reliability and psychometric quality for assessing problem behavior in children across cultures (Ivanova, Dobrean, et al., 2007). The validation of the Indonesian version of the CBCL/6-18 was obtained from a study involving 107 parents of children aged 6-18 in Central Java province. The Cronbach's alphas of the Indonesian version of the CBCL/6-18 ranged between .56 (Social problems) and .94 (Total Problems) (Ediati et al., submitted). These Cronbach's alphas were within the range of Cronbach's alphas obtained from 31 societies (Rescorla et al., 2007).

YSR. The YSR is a 119-item standardized self-report measure of emotional and behavioral functioning in youth aged 11 to 18 years (Achenbach & Rescorla, 2001). It comprised eight scales similar to CBCL, had been validated across 23 societies, and had satisfactory psychometric quality for assessing problem behavior among adolescents across cultures (Ivanova, Achenbach, et al., 2007). The validation of the Indonesian version of the YSR was obtained from a study involving 1154 high school students in Central Java province. The Cronbach's alphas of the Indonesian version of the YSR ranged between .62 (Social Problems) and .92 (Total Problems) (Ediati et al., submitted). To assess the

factor structure of the Indonesian translation of YSR, we followed procedures for confirmatory factor analysis described by Ivanova, Achenbach, et al. (2007) and found comparable results. The root-mean-square error of approximation (RMSEA) of .03 was within the range of Ivanova, Achenbach, et al. (2007) and indicated good fit. The comparative fit index (CFI) and Tucker-Lewis index (TLI) were .86 and .85 indicating acceptable fit (Ivanova, Achenbach, et al., 2007). The factor loadings ranged from .28 to .77 with median factor loading .57, whereas the factor covariance ranged from .45 to .98 with median covariance of .73. Thus, the results confirmed that the eight structure model also holds for the Indonesian translation of YSR (Ediati et al., submitted).

ASR. The ASR is a 131-item standardized self-report measure of emotional and behavioral functioning in adults aged 18 or older (Achenbach & Rescorla, 2003). It comprised eight scales: Anxious/Depressed, Withdrawn, Somatic Complaints, Thought Problems, Attention Problems, Aggressive Behavior, Rule-Breaking Behavior, and Intrusive (Achenbach & Rescorla, 2003). The validity and reliability of the Indonesian translation of the ASR were assessed following procedures described by Achenbach and Rescorla (2003). The data was obtained from a study involving 1091 university students in Central Java province. The Cronbach's alphas ranged from .59 (Thought Problems) to .94 (Total Problems). The RMSEA of .02 was within the range of Achenbach and Rescorla (2003) and indicated good fit. The CFI and TLI were both .90 indicating good fit (Achenbach & Rescorla, 2003). The factor loadings ranged from .17 to .78 with median factor loading .61, whereas the factor covariance ranged from .34 to .89 with median covariance of .63. The results confirmed that the eight-structure model also holds for the Indonesian translation of ASR (Ediati et al., submitted).

Socio-demographic characteristics. In addition to data on emotional and behavioral problems, we also collected data on socio-economic status, ethnic and cultural background, including age, gender, residence, ethnicity, religion, education (the highest level attained), and occupation.

Procedures

The study was carried out between March 2007 and May 2011. Following diagnostic procedures leading to the diagnosis of DSD (Juniarto et al., 2012), patients were invited to participate in this study. Oral and written study information was provided by a medical doctor (AZJ). After patients agreed to

participate and had given their written consent, an appointment was made for the study. The psychological assessment was conducted in the hospital or at home by a trained psychologist (AE). For participants younger than 18 years, written consent was obtained from the parents prior to assessment. All participants were assessed based on the gender they were living in (male or female) at the time of study. In subjects with limited educational background (i.e. illiterate) or unfamiliar self-report, the researcher administered ASEBA questionnaires orally. Similar to the paper-pencil version, the participants had to indicated their response (0-1-2) for each question which the researcher wrote their answer in the scoring sheet.

Statistical Analysis

Raw scores were used in comparison analysis between patients and matched control groups. To identify patients who were at risks for emotional and behavioral problems, the raw scores obtained were recoded into two categories: below or above the borderline cut-off points as defined by Achenbach & Rescorla (2001, 2003). The paired Wilcoxon sign-rank test was used to test differences in levels of emotional and behavioral problems between the patients and matched controls, whereas the McNemar test was used to test differences in individuals scoring above or below cut-points. Differences in percentage of subjects scored above and below cut-points were tested using the Fisher's Exact test. Differences were considered significant at $p < .05$ (two-sided). The effect size was calculated using *r* (for continuous data;

$r = \frac{Z}{\sqrt{n1+n2}}$) and *phi* ($\varphi = \sqrt{\frac{X^2}{N}}$ for categorical data).

Results

Participant characteristics

Table 2 summarizes the background of participants in this study. The patients and the matched control subjects did not differ with respect to socio-demographic and cultural variables. The majority of participants were male, lived in rural areas, came from the Central Java province, was Javanese and Moslem. The parents' educational background varied from illiterate to university level, the majority had attended high school. The only difference was found in

occupation; parents of patients more often worked in the lower-income sector or were unemployed.

Table 2 Socio-economic and cultural background of study participants

Characteristics	Patients with DSD (n = 118)	Matched Controls (n = 118)	p
Age of study	13.8 ± 7.4	14.2 ± 7.1	.69
Region			
Central Java province	100 (84.7)	108 (91.5)	.12
Other provinces in Java	12 (10.2)	9 (7.6)	
Outside Java island	6 (5.1)	1 (.8)	
Ethnicity			
Javanese	108 (91.5)	106 (89.8)	.82
Non Javanese	10 (8.5)	12 (10.2)	
Religion			
Islam	112 (94.9)	108 (91.5)	.44
Non Islam	6 (5.1)	10 (8.5)	
Education – Father*	n = 116	n = 114	
Illiterate	18 (15.5)	15 (13.2)	.62
Elementary school	38 (32.8)	31 (27.2)	
High school	49 (42.2)	58 (50.9)	
University education	11 (9.5)	10 (8.8)	
Education – Mother*	n = 116	n = 117	
Illiterate	22 (19.0)	14 (12.0)	.33
Elementary school	38 (32.8)	34 (29.1)	
High school	48 (41.4)	58 (49.6)	
University education	8 (6.9)	11 (9.4)	
Occupation – Father*	n = 116	n = 114	
Unemployed	6 (5.2)	5 (4.4)	.06
Labor	64 (55.2)	46 (40.4)	
Self-employed	19 (16.4)	34 (29.8)	
Staff / Office job	27 (23.3)	29 (25.4)	
Occupation – Mother*	n = 116	n = 117	
Unemployed	57 (49.1)	39 (33.3)	.02
Labor	32 (27.6)	35 (29.9)	
Self-employed	12 (10.3)	28 (23.9)	
Staff / Office job	15 (12.9)	15 (12.8)	

Note. Data presented in n (%), except age: in mean ± SD. The Fisher's exact test was applied; significant at $p < .05$.
* indicates differences in n.

Emotional and behavioral problems reported in children, adolescent, and adult participants

One parent of an adolescent with DSD did not complete the CBCL, consequently, data from the matched control was excluded from analysis. Therefore there was a discrepancy between the number of completed CBCL (n = 46) and YSR (n = 48). Table 3 gives the results of comparison between patients

and matched control groups on parental and self-reports (CBCL, YSR, and ASR).

Children. Parents of children with DSD reported more emotional and behavioral problems in their children than parents of the matched control children did (Total Problems: $p = .02$), particularly in Social Problems ($p = .04$), Attention Problems ($p = .03$), Aggressive Behavior ($p = .02$), and Externalizing Problems ($p = .03$). No significant differences were found in other scales (see Table 3a).

Table 3.a. Emotional and behavioral problems reported among **parents of children aged 6-11**

CBCL/6-18 scales	Patients with DSD	Matched controls	*p*	ES
	n = 60	*n* = 60		
Anxious/Depressed	1 (0-7)	1 (0-9)	.59	-.01
Withdrawn/Depressed	1.5 (0-12)	1 (0-10)	.43	-.13
Somatic complaints	1 (0-6)	0 (0-8)	.64	-.05
Social problems	3 (0-10)	2 (0-11)	**.03**	-.18
Thought problems	1 (0-6)	0 (0-8)	.83	-.01
Attention problems	2 (0-10)	1 (0-9)	**.01**	-.20
Rule-breaking behavior	1.5 (0-13)	1.5 (0-8)	.54	-.11
Aggressive behavior	4 (0-24)	2 (0-18)	**.05**	-.21
Internalizing problems	3 (0-18)	4 (0-23)	.52	-.07
Externalizing problems	5 (0-35)	3 (0-22)	.09	-.20
Total problems	18 (3-49)	11 (0-57)	**.04**	-.21

Note. CBCL = Child behavior checklist. ES = effect size (*r*). Data presented in Median (range). Higher scores indicate more problems. The paired Wilcoxon signed-rank test applied; significant at $p < .05$

A separate analysis by gender was conducted and showed that parents of boys with DSD reported more problems than parents of the matched control boys (Total Problems: $Mdn_P = 22.0$; $Mdn_C = 13.0$; $p = .05$), particularly in Aggressive Behavior ($Mdn_P = 5.5$; $Mdn_C = 3.0$; $p = .02$) and Externalizing Problems ($Mdn_P = 7.5$; $Mdn_C = 5.0$; $p = .04$). In contrasts, no significant differences on CBCL scores were found between parents of girls with DSD and of the matched control girls.

Adolescents. In Table 3b we present the results of comparison of parental report on adolescents emotional and behavioral problem (CBCL), and present the comparison results of the adolescent self-report (YSR) in Table 3c. We did not find significant differences on the CBCL and YSR scores between the patients and the matched control groups (see Table 3b and 3c).

Table 3.b. Emotional and behavioral problems reported among parents of adolescents aged 12-17

CBCL/6-18 scales	Patients with DSD	Matched controls	*p*	ES
	n = 23	*n* = 23		
Anxious/depressed	1 (0-5)	1 (0-5)	.61	-.01
Withdrawn/depressed	2 (0-7)	1 (0-6)	.11	-.21
Somatic complaints	0 (0-4)	1 (0-8)	.22	-.08
Social problems	3 (0-7)	2 (0-10)	.75	-.30
Thought problems	0 (0-2)	0 (0-4)	.85	-.02
Attention problems	1 (0-9)	1 (0-9)	.73	-.32
Rule-breaking behavior	1 (0-6)	1 (0-4)	.58	-.18
Aggressive behavior	5 (0-14)	2 (0-14)	.18	-.34
Internalizing problems	3 (0-11)	2 (0-19)	.68	-.11
Externalizing problems	6 (0-15)	4 (0-16)	.27	-.32
Total problems	16 (3-29)	13 (1-45)	.22	-.34

Note. CBCL = Child behavior checklist. ES = effect size (*r*). Data presented in Median (range).

Higher scores indicate more problems. The paired Wilcoxon signed-rank test applied; significant at $p < .05$

Table 3.c. Emotional and behavioral problems reported among adolescents aged 11-17 years

YSR scales	Patients with DSD	Matched controls	*p*	ES
	n = 24	*n* = 24		
Anxious/Depressed	1.5 (0-10)	2 (0-19)	.55	-.09
Withdrawn/Depressed	2 (0-13)	2.5 (0-9)	.60	-.08
Somatic complaints	1 (0-9)	0 (0-7)	.46	-.11
Social problems	2.5 (0-10)	3 (0-14)	.99	0
Thought problems	0 (0-6)	0 (0-10)	.85	-.03
Attention problems	2.5 (0-13)	3.5 (0-15)	.99	0
Rule-breaking behavior	1 (0-10)	2 (0-7)	.36	-.14
Aggressive behavior	3 (0-13)	3 (0-16)	.52	-.10
Internalizing problems	5 (0-25)	5.5 (0-35)	.51	-.10
Externalizing problems	4 (0-21)	5.5 (0-21)	.74	-.13
Total problems	17 (3-60)	18.5 (0-96)	.84	-.03

Note. YSR = Youth self-report. ES = effect size (*r*). Data presented in Median (range).
Higher scores indicate more problems. The paired Wilcoxon signed-rank test applied; significant at $p < .05$

Adults. As reported in the Table 3d, adults with DSD reported more Anxious/Depressed and Internalizing Problems than the matched control adults ($Mdn_P = 9.0$; $Mdn_C = 5.0$; $p = .01$; $Mdn_P = 15.5$; $Mdn_C = 10.5$; $p = .04$, respectively). Men with DSD rated themselves higher on the Anxious/Depressed scale than the matched control men ($Mdn_P = 6.5$; $Mdn_C = 2.5$; $p = .04$), but not in other problems scales. Women with DSD rated themselves higher on the Withdrawn scale than the matched control women did ($Mdn_P = 6.0$; $Mdn_C = 3.5$; $p = .02$), but not in other problem scales.

Table 3.d. Emotional and behavioral problems reported among adults aged 18 or above

ASR scales	Patients with DSD (n = 34)	Matched Controls (n = 34)	p	ES
Anxious/Depressed	9 (0-34)	5 (0-26)	**.02**	-.29
Withdrawn	4 (0-16)	2.5 (0.10)	.10	-.22
Somatic complaints	1 (0-10)	1 (0-12)	.56	-.08
Thought problems	2 (0-8)	2 (0-9)	.53	-.07
Attention problems	4 (0-21)	5.5 (0-19)	.32	-.12
Aggressive behavior	6 (0-21)	5 (0-15)	.45	-.11
Rule-breaking behavior	1 (0-12)	1.5 (0-7)	.99	-.01
Intrusive	1 (0-9)	1 (0-7)	.96	-.02
Internalizing problems	14 (0-53)	9.5 (0-45)	**.03**	-.25
Externalizing problems	8 (1-36)	8 (0-25)	.59	-.06
Total problems	29.5 (2-110)	27 (1-91)	.10	-.18

Note. ASR = Adult self-report. ES = effect size (r). Data presented in Median (range). Higher scores indicate more problems. The paired Wilcoxon signed-rank test applied; significant at $p < .05$

Patients with DSD who are at risk for emotional and behavioral problems

Comparison between patients with DSD and the matched control subjects who scored in the borderline and clinical ranges (Achenbach & Rescorla, 2001, 2003), that is, above the borderline cut-off points. The findings did not show any significant differences on all scales. Figure 1 showed the percentage of patients and the matched controls who scored in the borderline and clinical ranges. Withdrawn/Depressed, Internalizing Problems and Externalizing Problems are mainly reported in both patients and matched control groups.

Subsequently, we made comparisons between different subgroups of patients: patients with different DSD diagnosis, patients from different age groups, patients who had received treatment and patients who had not, patients who had undergone a change in social gender role or had changed their social gender role themselves. The results are demonstrated in Figure 2 and Table 4-5.

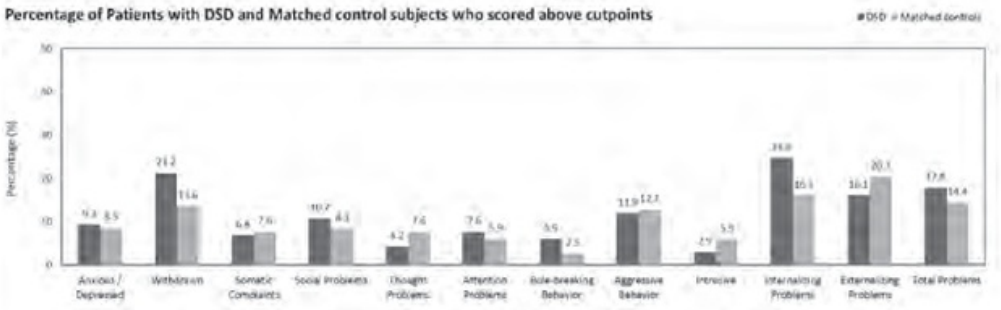

Figure 1. Percentages of patients and matched controls who scored above the borderline cut-off point in the ASEBA scales

Note. The cut-points were based on Achenbach & Rescorla (2001, 2003). The McNemar test was applied; significant at $p < .05$.
p = n.s. in all scales

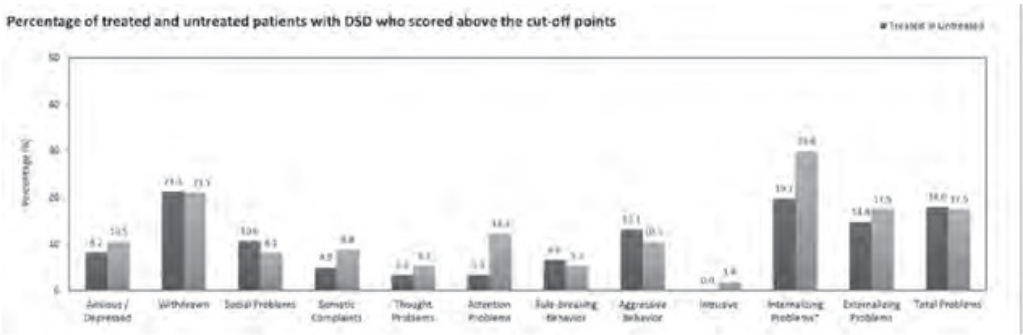

Figure 2. Percentages of treated and untreated patients with DSD who scored above the borderline cut-points in the ASEBA scales

Note. N=118, except in the Social Problems (n = 84; only available in the CBCL and YSR) and Intrusive scales (n = 34; only in the ASR).
The cut-points were based on Achenbach and Rescorla (2001, 2003). The Fisher Exact test was applied; significant at $p < .05$.
* p = .047 (results of the Fisher's Exact for Internalizing problem)

Treated vs untreated patients. Figure 2 shows the percentages of treated and untreated patients who scored in the borderline and clinical range. Untreated patients more often reported internalizing problems than treated patients (29.8% versus 19.7%; p = .047), whereas both treated and untreated patients reported they withdraw themselves from their social contacts (approximately 21%, in both groups).

Patients with a history of social gender role change vs patients who did not change gender. We compared groups of patients with and without a history of social gender role change and found no significant differences in all scales

measured. Among 21 patients who underwent a social gender role change, eight patients (38%) reported internalizing problems and seven (33.3%) reported withdrawn problems within borderline and clinical range. Among patients who did not change their social gender role the percentages were 21,6% and 18.6%, respectively, on Internalizing problems and Withdrawn problems. In the matched control group the percentages were 16% and 13.6% on these scales.

Age group comparison. Table 4 shows the number of children, adolescents, and adults with DSD who scored in borderline and clinical ranges. Significant differences were found in problems related to Anxious/Depressed, Thought Problems, Internalizing Problems, and Externalizing Problems. Except in Externalizing Problems, adult patients more often had scores in the borderline and clinical ranges than younger patients did. Externalizing Problems were prominent among 23.3% of children with DSD. There were 25 patients (21.2%) who scored in the borderline and clinical ranges of the Withdrawn/Depressed scale but there were no significant difference across age groups. Similar analysis in the matched control group revealed no significant differences across age groups on all scales.

Table 4 Comparison among children, adolescents, and adults with DSD who are scored above cut points

Scales	Children (*n* = 60)	Adolescents (*n* = 24)	Adults (*n* = 34)	*p*	ES
Anxious/depressed	1 (1.7)	0	10 (29.4)	**< .001**	.00
Withdrawn/depressed	11 (18.3)	3 (12.5)	11 (32.4)	.16	.04
Somatic complaints	1 (1.7)	3 (12.5)	4 (11.8)	.20	.02
Social problems [a]	7 (11.7)	2 (8.3)	-	.99	.09
Thought problems	1 (1.7)	0	4 (11.8)	**.046**	.02
Attention problems	3 (5.0)	1 (4.2)	5 (14.7)	.24	.04
Rule-breaking behavior	5 (8.3)	1 (4.2)	1 (2.9)	.59	.07
Aggressive behavior	10 (16.7)	1 (4.2)	3 (8.8)	.26	.05
Intrusive [b]	-	-	1 (2.9)	-	-
Internalizing problems	9 (15.0)	4 (16.7)	16 (47.1)	**.003**	.00
Externalizing problems	14 (23.3)	0	5 (14.6)	**.02**	.02
Total problems	11 (18.3)	3 (12.5)	7 (20.6)	.73	.08

Note. ES = Effect size (Cramér's phi/φ_c). Data presented in *n* (%). The Fisher Exact test was applied; significant at $p < .05$

[a] $n = 84$. The social problem scale was only available in the CBCL and YSR.

[b] $n = 34$. The intrusive scale was only available in the ASR.

Table 5 Percentages of patients with different DSD diagnoses who scored above the borderline cut-off points

Scales	CAH-SV (*n* = 24)	Gonadal dysgenesis (*n* = 35)	AIS (*n* = 16)	Androgen Action Disorder (*n* = 22)	Undermasculinization unknown cause (*n* = 19)	*n* (%)	*p*	ES
Anxious/depressed	1 (4.2)	4 (11.4)	2 (12.5)	2 (9.1)	1 (5.3)	10 (8.6)	.84	.08
Withdrawn	9 (37.5)	7 (20.0)	1 (6.2)	5 (22.7)	2 (10.5)	24 (20.7)	.14	.03
Somatic complaints	3 (12.5)	2 (5.7)	0	1 (4.5)	0	6 (5.2)	.48	.05
Social problems [a]	2 (10.0)	1 (5.3)	2 (20.0)	3 (15.8)	1 (6.7)	9 (7.7)	.70	.09
Thought problems	1 (4.2)	1 (2.9)	1 (6.2)	1 (4.5)	0	4 (3.4)	.91	.09
Attention problems	0	3 (8.6)	1 (6.2)	2 (9.1)	2 (10.5)	8 (6.8)	.58	.08
Rule-breaking behavior	1 (4.2)	0	2 (12.5)	2 (9.1)	1 (5.3)	6 (5.2)	.18	.06
Aggressive behavior	2 (8.3)	5 (14.3)	1 (6.2)	3 (13.6)	2 (10.5)	13 (11.2)	.94	.09
Intrusive [b]	0	1 (6.2)	0	0	0	1 (0.9)	.99	.17
Internalizing problems	6 (25.0)	9 (25.7)	4 (25.0)	5 (22.7)	4 (21.1)	28 (24.1)	.99	.09
Externalizing problems	3 (12.5)	6 (17.1)	2 (12.5)	5 (22.7)	2 (10.5)	18 (15.5)	.86	.08
Total problems	3 (12.5)	6 (17.1)	3 (18.8)	6 (27.3)	2 (10.5)	20 (17.2)	.68	.08

Note. Data were presented in *n* (%). N=116 (two patients with Cloacal exstrophy were not included). The Fisher Exact test was applied; significant at $p < .05$. Cut-off point applied was referred to the index in the manual (Achenbach & Rescorla, 2001, 2003). CAH-SV = simple virilizing type of congenital adrenal hyperplasia; AIS = androgen insensitivity syndrome. ES = Effect size (Cramér's phi/φ_c)

[a] The Social Problem scale is only available on CBCL and YSR (*n* = 83).

[b] The Intrusive scale is only available on ASR (*n* = 33).

Diagnoses comparison. Considering the sample size discrepancy across diagnoses, we did not include patients diagnosed with cloacal exstrophy (n = 2) for comparison analysis. Subsequently, we compared patients diagnosed with congenital adrenal hyperplasia/CAH (n = 24), gonadal dysgenesis (n = 35), androgen insensitivity syndrome/AIS (n = 16), disorder in androgen action/AAD (n = 22), and patients with undermasculinization in whom the cause remained unknown (n = 19). Table 5 showed patients with different DSD diagnoses who scored above cut-off points across the scales. The results showed no significant differences on all scales across different diagnostic groups.

Internalizing problems were largely reported among 21-26% of patients with different diagnostic groups. Withdrawn problems were often reported among patients diagnosed with 46,XX CAH-SV (9 patients or 37.5%), Androgen Action Disorder (5 patients or 22.7%), and Gonadal dysgenesis (7 patients or 20%). In addition to these findings, comparison between young girls with CAH and the matched controls girls (aged 6-11) showed no significant differences in all CBCL scales, except in the Withdrawn/Depressed scale. Girls with CAH withdrawn themselves more often than the matched control girls did (Mdn_P = 3.0; Mdn_C = 1.0; p = .03).

Discussion

This study aimed to investigate emotional and behavioral problems reported among Indonesian children, adolescents, and adults with DSD. We observed that parents of children with DSD observed more emotional and behavioral problems in their children than parents of control children did. Social problems, attention problems, aggressive behaviors, and externalizing problems were more frequently rated among children with DSD than the matched control children. In contrast, adolescent patients and their parents did not report specific emotional and behavioral problem, whereas adults patients more often reported specific problems in anxiety and internalizing behaviors than the matched control adults. No significant differences were found in comparison across different DSD diagnoses. However, the parents of young girls with CAH reported their daughters withdrew themselves from social activities more frequently than the matched control girls did, according to parental reports.

The parents of young boys with DSD had more emotional and behavioral problems, externalizing problems and aggressive behavior than the matched controls boys, whereas such differences were not found among young girls with DSD. This finding was similar to some extent with a study from China which reported more behavioral problems among young boys with DSD, but different types of problems were observed (Zhu, et al., 2010). Chinese young boys with DSD were more depressed than their matched controls whereas parents did not observe significant differences between young girls with DSD and their matched control girls (Zhu, et al., 2010). Compared to matched control adults, adult men with DSD reported more anxiety and depression, whereas women with DSD more frequently withdraw themselves from social activities, A study done by Migeon et al. (2002) on individuals with XY DSD that reported 38% men and 28% women had received counseling due to depression. Unfortunately, study on emotional and behavioral problems among adults with DSD are scarce and study on emotional and behavioral problems among general population of Indonesia was not available. This makes us difficult to justify our findings.

This study is unique as it comprised 48,3% of patients who had been left untreated until recently, when they came to our hospital. The remaining 51,7% of patients had received some hormonal medication or had undergone some genital surgery. These patients had to live with ambiguous genitalia and bodies that had an ambiguous appearance, often leading to ambiguity in gender. They also had to live with a lack of knowledge about their condition and without sufficient medical help. All these factors make it difficult to cope with the condition and may put patients at risk for developing emotional problems. Our data showed that, either treated or untreated, patients more often withdrew themselves from social activities, however, untreated patients exhibited more internalizing problems than the treated patients. Patients who had received some medical treatment in our center differ from the untreated patients in way that they had received more information about their DSD condition through genetic and psychological counseling as well as several meeting with a multidisciplinary team that specialized in DSD. This team offered patients and their relatives the opportunity to discuss their concern and problems related with their DSD condition. However, the reported problems of social withdrawal indicates the need for improving patients' skill in dealing with social situation. Such social skill training should be designed as practical as it closely related to their daily lives and may be integrated into the psychological treatment plan for a long-term follow-up.

The ASEBA measures applied in this study enable us to identify subjects who scored within the borderline range that are sufficient to be of concern to consider the need for professional help (Achenbach & Rescorla, 2001, 2003). Our study indicates that approximately a quarter of all patients (25%) experienced internalizing problems. They particularly reported to be withdrawn/depressed (21%). Adults, particularly patients who never received medical treatment for their DSD condition, reported more internalizing problems than patients who had received some treatment. Men and women with DSD reported different type of problems compared to the matched control adults: men reported more anxiety and depression whereas women reported to be more withdrawn. Our findings are in line with previous findings on sexuality that revealed sexual distress, fear of rejection, and avoidance to enter romantic relationship among women with DSD in Indonesia (Ediati, et al., 2013a). Applying a standardized measure was helpful to identify these emotional problems. The study also revealed that there is a substantial proportion of patients who suffer and need psychological or psychiatric help to alleviate these problems and help them coping with their condition in daily life. These findings underline the importance of early referral to a specialized, multidisciplinary team that need to be promoted for all individuals suspected with DSD. In addition to medical treatments, this team should offer education and psychological counseling, to improve understanding of the condition by the patients and their family, and to improve acceptance and support for patients with DSD and the parents.

This study reports no significant differences in emotional and behavioral problems between adolescents with DSD and the matched control adolescents in problem behavior, either reported by parents or adolescents themselves. This finding is contrary to our expectation as a recent survey in Indonesian young adults revealed that their initial cigarette smoking, drinking, drug use, dating, and premarital sex were happened during adolescence (Badan Pusat Statistik (BPS)-Statistics Indonesia & Macro International, 2008). Therefore, we initially assumed that some behavioral problems would be reported among adolescents. Our findings are similar with findings reported by Kleinemeier and colleagues (2010) who also did not found any significant differences in emotional and behavioral problems between the adolescents with DSD and the healthy adolescents. They assumed that the absence of difference was due to the advance of medical treatment. It is interesting that we found similar finding in our study that comprised 41.7% (10 out of 24) adolescents with DSD

who never received any medical treatment. In another study on quality of life among adolescents with DSD, we also found no significant differences between adolescents with DSD and their matched controls. We assumed that adolescence characteristics and culture may explain this findings. In adolescence, peer influence and pressure become stronger than in childhood and a collective-driven culture like Indonesia may impose greater social influence particularly on teenagers. As a result, adolescents are more conform to the peers expectation than before. The absence of significant differences did not indicate the absence of emotional and behavioral problems because some degree of problems were reported in all scales of YSR, except in Thought Problems. Despite this finding, a follow-up psychological evaluation is necessary for these adolescents with DSD. A previous study on gender development and sexual functioning among Indonesian adult patients with DSD indicated that patients who had undergone a social gender role in adulthood, experienced gender identity problems and difficulties to deal with sexual attraction since adolescence (Ediati, et al., 2013a, 2013b). Patients with DSD are confronted with their condition during adolescence as sexuality and gender becomes more important than it has been in childhood. With respect to gender, gradually, society expects adolescents to behave themselves according to men and women. Adolescents with DSD may experience a conflict with social expectations they do not want or cannot fulfill. For instance they may become aware that their assigned gender may not fit well; they become aware about society's demands on reproduction and the adverse position of the infertile or homosexual adult.

We assessed differences on reported emotional and behavioral problem among patients with different diagnostic groups and found no significant differences. Internalizing problems were largely reported among patients, regardless DSD diagnoses. Patients with 46,XX CAH, androgen action disorder, and gonadal dysgenesis often withdrawn themselves. These findings indicate that emotional and behavioral problems reported among patients with DSD are not diagnose-specific. Our findings on children with CAH did not support previous reports (Oner et al., 2010; Pasterski et al., 2007) who found more behavioral problems in girls with CAH than the matched control girls. Different type of problems were found among young girls with CAH in this study: they were more withdrew themselves from social activities than the matched control girls did. Difficulties to accept the DSD condition or fear that DSD being uncovered by others possibly explained their tendency to withdrawn

themselves and therefore internalizing problems were more prominent.

This study has several limitations. First, the small sample size prevented us from further stratified comparison analysis. Such limitation is often encountered in clinical studies involving patients with rare conditions. For example we could not assess differences in patients with 46,XY complete AIS and patients with 46,XY partial AIS or patients with 46,XX CAH raised as girls and those raised as boys. Second, this is the first study on patient reported outcomes on emotional and behavioral problems in an Indonesian sample. Most Indonesians are not experienced in self report measures, particularly less educated and less prosperous Indonesians do not have such experiences. Although preliminary data on psychometric properties of the translated ASEBA questionnaire are satisfying, we need more data from various Indonesian populations to confirm these findings.

In conclusion, we identified emotional and behavioral problems among a majority of Indonesian patients with DSD who were identified late in life. Children and adults with DSD reported more emotional and behavioral problems than their matched controls. Internalizing problems were evident among patients, particularly untreated patients, and not diagnose-specific. Approximately 25% of patients reported serious emotional and behavioral problems that need to be attended. These data show that it is difficult for patients to cope with their condition, therefore, psychological intervention to reduce these problems should be integrated into the treatment plan. Psychological long term follow-up is imperative, particularly during and after adolescence. Early referral and early identification of DSD is necessary and should be promoted among health practitioners in the primary care centers.

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Chapter 6

Social stigmatization in Indonesian patients with disorders of sex development

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Abstract

Background. Persons with disorders of sex development (DSD) may be vulnerable for social stigmatization but studies in this field are scarce. Treatment of patients with DSD in Indonesia has become available only recently. Consequently, many patients with DSD have been living in ambiguity of gender and bodies for most of their lives. We assess the stigmatization towards persons with DSD as reported by adults and parents of children and adolescents with DSD.

Methods. 118 patients with DSD (60 children, 22 adolescents, 34 adults), aged 6-41, participated in this study. The Social Stigmatization Scale towards DSD (SSS-DSD) was developed and applied in this study. A mixed-method was applied to obtain quantitative and qualitative data from parents and adults. Differences in reported stigmatization were explored across gender, residential settings, treatment status, and visibility of DSD characteristics.

Findings. Patients with a visible DSD characteristics, female, and living in rural areas were at risk for social stigmatization. Ambiguity in the genitalia, the body and in gender role behavior, elicited social stigmatization. Emotional problems were reported by patients who experienced stigmatization as well as by patients who anticipated stigmatization. We found five themes that explain stigmatization and stress: lack of knowledge on DSD, patient's and society's characteristics, patient's response towards the environment, and society's response to patients with DSD.

Conclusion. Patients with a DSD are vulnerable to stigmatization. Education about DSD and how to cope with stigmatization are necessary. Reliable information about DSD should be made available not only for patients and parents, but also for laymen.

Keyword stigma, disorders of sex development, late treatment, Indonesia

Background

Disorders of sex development (DSD) refer to a group of congenital conditions in which development of chromosomal, gonadal, or anatomical sex is atypical, leading to an ambiguous body and appearance.[1] In Western countries, it is assumed that ambiguity in physical appearance may lead to social stigmatization, and will affect the patients' psychosocial well-being. Part of the available treatments are aimed to reduce or even prevent stigmatization; hormonal treatments, gonadectomy, and genital surgeries can reduce physical ambiguity and enable sexual functioning. Application of these treatments would increase patient's opportunities for social participation. This practice started many years ago. Despite criticism on particular genital corrections, many children born with ambiguous genitals undergo genital correction. They also choose gonadectomy to prevent pubertal development of an ambiguous body. This makes it difficult to investigate potential social stigmatization due to body ambiguity in Western DSD patients.

In the medical literature, only a few reports on stigmatization on patients with DSD can be found, and these are case reports or did not specifically aimed to focused on stigmatization.[2-5] Moreover, those reports focused on Asian patients from Vietnam, India and Malaysia rather than patients living in Western societies.

DSD is not widely known among the general population in Indonesia, not even among health practitioners. Only recently, awareness about DSD was promoted through scientific meetings for medical doctors and an education program for genetic counselors. Clinical management of patients with DSD in Indonesia had been challenged given the limited diagnostic and treatment facilities, health practitioners' expertise, and lack of awareness on DSD. Prior to this study, we have been confronted with patients who reported hostile reactions , fear of ostracism, and this was the reason why we initiated a study on the stigmatization on persons with DSD in Indonesia. We aim to assess patients' experiences with stigmatization due to their DSD condition and the stress level evoked by such experiences. We addressed the following research questions: Do Indonesian patients with DSD experience social stigmatization? How stressful is the stigmatization for adult patients and youngsters with DSD? What type of stigmatization do they report and what is the context of occurrence?

Methods

Study design

This is a cross sectional study to assess patients' experiences with stigmatization due to DSD. Between March 2007 and May 2011, we collected data on the frequency of stigmatization experience and how stressful it was for patients. Furthermore, we gathered collected patient's opinions and reactions on the reported stigmatizing experiences to support the explanation of the quantitative data.[6] The study protocol had been approved by the board of the ethical committee from the Faculty of Medicine Diponegoro University (FMDU), Semarang, Indonesia.

Patients

All patients with a proven diagnosis of DSD[7-8] who were under clinical management of the Sexual Adjustment Team, of the Dr. Kariadi Hospital/FMDU were invited for study participation. All included patients had given their informed consent after they had received oral and written study information was provided by a medical doctor (AZJ). Excluded were individuals with 46,XY and 46,XX DSD and features suggestive of a dysmorphic syndrome, patients with sex chromosome DSD without mosaicism, and patients with DSD and intellectual disabilities (indicated from the child's academic achievements and/or observed by the medical doctor in interaction with the patient). Thirty-four adults (20 men; 14 women; aged 18-41 years) and 81 parents of 60 children (42 boys, 18 girls; aged 6-11) and 21 adolescents (15 boys; 6 girls; aged 12-17 years) took part in the study. Table 1 summarizes the types of DSD diagnoses of patients in this study.

Procedures

Prior to study onset, no measure was available to assess social stigmatization in patients with DSD. Therefore, we developed measure specific for the study: the Social Stigmatization Scale for DSD (SSS-DSD). The SSS-DSD contains 15 questions to assess the frequency of stigmatization experienced and the level of stress-level evoked by the stigmatizing experiences. A 5-option Likert scale was provided as response mode ranging from '*not at all*' (1) to '*very much*' (5). In addition we asked patients to explain about their experiences, give examples. We asked a few questions about their cognitions on the cause of DSD (do you believe in *'kutuk'* (a curse); do you believe that the genital anomaly is caused by parental sins? Or due to taken food or display actions forbidden during pregnancy), worries,

and inability to cope with DSD. We developed separate versions for parents and adult reports. The parental version of the SSS-DSD is similar to the adult version and assesses the parent reports on children or adolescents with DSD. SSS-DSD adult and parents versions are presented in table 3.

Table 1 DSD diagnoses of participants in the study (N=115)

DSD diagnoses	Children	Adolescents	Adults	Total
46,XX CAH-SV [a]	18	1	4	23
AIS [b]	5	5	6	16
Gonadal dysgenesis [c]	12	5	16	33
Cloacal Malformation	-	1	1	2
Androgen action disorder (AAD) [d]	13	6	3	22
Under masculinization unknown cause [e]	12	3	4	19
Total	60	21	34	115

[a] CAH-SV: simple virilizing type of congenital adrenal hyperplasia. CYP 21 mutation was confirmed (Juniarto, 2013).
[b] AIS: androgen insensitivity syndrome. AR gene mutation was confirmed (Juniarto, 2013).
[c] A condition in which patients had abnormal hormonal testicular function with uni/bilaterally undescended testes. Androgen action was presumed to be fully effective. The clinical and biochemical presentation suggest gonadal dysfunction. Serum levels of luteinizing hormone and follicle stimulating hormone were elevated but testosterone, anti-müllerian hormone, and Inhibin are low for age, and no or diminished serum testosterone response to HCG. Including in this group is patients with chromosomal DSD
[d] 46,XY DSD and disorder in androgen action. All subjects had undervirilisation (EMS < 9) and normal hormonal testicular function with uni/bilaterally undescended testes. We presume, in these patients, androgen actions not to be fully effective. The clinical and biochemical presentation were close to those of subjects with a mutation in the androgen receptor with elevated serum levels of luteinizing hormone, levels of testosterone, and anti-müllerian hormone but a mutation in the androgen receptor but a mutation in the androgen receptor could not be confirmed despite extensive analysis (Juniarto, 2013).
[e] Under masculinization unknown cause refers to 46,XY DSD male undermasculinization (EMS > 9) with unknown cause could be identified despite extensive analyses. Serum hormone values and response to HCG were all normal for age.

Prior to implementation, the SS-DSD was tested in a pilot study to test the applicability. We concluded that application of the measure as a paper-pencil test was feasible for well-educated subjects who were also familiar with self-report, whereas the measure should preferably applied orally as a structured interview for illiterate subjects or subjects with low educational levels and unfamiliar with self-reports. Patients' opinions and reactions were written down by the researcher. In addition to data on stigmatization, we collected data on patient's socio-economic and ethnic-cultural background. After parents and adult patients had given their written consent, an appointment was made for the psychological study in the hospital or at the patient's home. The psychological study was conducted by a trained psychologist (AE).

Data analysis

Construct validity of both the adult and parental versions of the SSS-DSD scale was explored using principal component analysis (PCA) with varimax rotation and Kaiser normalization method. Factors with Eigen values greater than 1 and items with factor loadings (after rotation) greater than .40 were considered acceptable. Instrument reliability was evaluated as internal consistency with Cronbach's Alpha as outcome measure.

The overall and domain sum scores of the SSS-DSD were calculated as the unweighted sum scores of the individual domains and items, respectively. Spearman's correlation coefficient (*rho*) was applied to evaluate the correlations between different types of experienced stigma and stress evoked by stigmatized experience. The Kruskal-Wallis test was applied to test the difference in continuous data of more than two groups, whereas differences between two independent groups were tested using the Mann-Whitney U test. Differences in categorical data were compared using Fisher's Exact test. Differences were considered significant at $p < .05$ (two-sided).

For the qualitative data, respondents' responses on the open-ended questions were translated into English. We then performed an inductive content analysis using NVIVO qualitative data analysis software.[9-11] The open coding procedure resulted in many codes that were clustered into five broader themes.[9] For reliability analysis, we used the inter-coder reliability[12] using three independent coders (AE, AC, AD) who used five themes to code 12 different subsets of dataset representing the variety in the samples (10% of the entire sample). The inter-rater reliability was calculated using the 'compare coding' application in NVivo's[10-11]. The average percentage of agreement among three raters reached 91%. Next, the remaining dataset was coded according to these five themes. Relationships between themes were investigated using the compound coding application in NVivo[10-11] .

Results

The majority of participants was male, lived in rural areas,, was Javanese and Moslem, parents' educational background varied from illiterate to university level, the majority had attended high school and worked in the lower-income sector or were unemployed. Details on socio-economic and ethnic-cultural variables can be found in Table 2.

Table 2 Participant characteristics (N=115)

Characteristics	Children and adolescents (*n*=81)	Adults (*n*=34)
Gender (of patients)		
Male	57 (70.4)	20 (58.8)
Female	24 (29.6)	14 (41.2)
Treatment		
Received treatment [a]	44 (54.3)	15 (44.1)
No treatment	37 (45.7)	19 (55.9)
Social gender role change		
Yes	7 (8.6)	15 (44.1)
No	74 (91.4)	19 (55.9)
Visibility of DSD [b]		
Visible	12 (14.8)	17 (50.0)
Partly hidden	57 (70.4)	17 (50.0)
Hidden	12 (14.8)	
Region		
Central Java	70 (86.4)	29 (85.2)
Other provinces in Java	8 (9.9)	2 (5.9)
Outside Java island	3 (3.7)	3 (8.8)
Ethnic		
Javanese	76 (93.8)	31 (91.2)
Non Javanese	5 (6.2)	3 (8.8)
Religion		
Islam	77 (95.1)	33 (97.1)
Non Islam	4 (4.9)	1 (2.9)
Residential setting		
Rural	45 (55.6)	15 (44.1)
Suburban	24 (29.6)	11 (32.4)
Urban	12 (14.8)	8 (23.5)
Highest education attained	(Fathers* / Mothers*)	(Adults)
Illiterate	9 (11.3) / 10 (12.5)	4 (11.8)
Elementary school	27 (33.7) / 28 (35.0)	3 (8.8)
High school	36 (45.0) / 36 (45.0)	23 (67.6)
University	8 (10.0) / 6 (7.5)	4 (11.8)
Parents' occupation	(Fathers* / Mothers*)	(Adults)
Unemployed	0 / 44 (55.0)	13 (38.2)
Labor	47 (58.7) / 22 (27.5)	9 (26.5)
Self employed	16 (20.0) / 6 (7.5)	4 (11.8)
Staff	17 (21.3) / 8 (10.0)	8 (23.5)

Note. Data are presented in *n* (%) * One father/mother missing for being deceased.

[a] Treatment in most patients had been minimal.

[b] Refers to degree of visibility of DSD characteristics for other people; Visible DSD refers to DSD characteristics that obviously recognized by others or already known publicly (i.e. ambiguous body, genital, behavior); partly hidden DSD refers to DSD characteristics that are covered but possibly known by others (e.g. hypospadias, male with developed breasts, women with no breasts); hidden DSD refers to DSD condition that will not be identified by others, unless it was disclosed (e.g. women with CAIS)

Validity and reliability of SSS-DSD parental and adult versions

SS-DSD Parent-report. The principal component analysis (PCA) extracted four components explaining 56% of the total variance: a) stigmatization elicited by genital ambiguity (items 1-2, 5-6, 11; α = .86); b) stigmatization elicited by

ambiguous body appearance or behavior (items 3- 4, 7-8a; α = .84); c) social rejection (items 9-10, 12; α = .88); and d) emotional problem due to DSD (items 13a-d, 13g-h; α = .85). Table 3 and 3b shows the factor loadings after varimax rotation and the Cronbach's alpha of each component. The construct validity and reliability of the SS-DSD Parental–Report was considered satisfactory.

SSS-DSD Adult-Report. The PCA extracted three components explaining 62.9% of the total variance: a) verbal stigmatization (items 1-2, 4-5, 7; α = .92); b) behavioral stigmatization (items 3, 6a, 9-10; α = .85); and c) emotional problems due to DSD (items 13-15; α = .94). Table 4 shows the factor loadings after varimax rotation and the Cronbach's alpha of each component. The construct validity and reliability of the SSS-DSD Adult-Report was also considered satisfactory.

Correlations between stigmatization and stress

In both measures, items measuring experiences with stigmatization were positively and significantly correlated with items measuring stress evoked by such stigmatization, in all components measured.

SSS-DSD Parent-report. Stigmatization due to genital ambiguity positively correlated with stress (r_s (79) = .794, $p < .001$); stigmatization elicited by an ambiguous appearance or behavior positively correlated with stress (r_s (79) = .80, $p < .001$); social rejection positively correlated with stress (r_s (79) = .81, $p < .001$); and emotional problems also positively correlated with stress (r_s (79) = .64, $p < .001$).

SSS-DSD Adult-Report. Verbal stigmatization positively correlated with stress (r_s (32) = .755, $p < .001$); behavioral stigmatization positively correlated with stress (r_s (32) = .753, $p < .001$); and emotional and acceptance problems due to DSD also positively correlated with stress (r_s (32) = .882, $p < .001$). The more frequent patients reported experiences with stigmatization, the higher the reported stress evoked by these experiences.

Table 3a Factor loadings after varimax rotation and Cronbach's alphas of the SSS-DSD Parental report (N = 81)

Questions	Components			
	1[a]	2[b]	3[c]	4[d]
01a. Can other people see that your child got a genital that is (slightly) different from that of other children?	**.60**	.44	.07	-.14
01b. How stressful is this to you?	**.72**	.22	.31	-.09
02a. Do you think that other people look at your child because of the ambiguous genital?	**.64**	.38	-.05	.19
02b. How stressful is this to you?	**.73**	.13	.17	.21
05a. Do other people speak negatively about *your child* because of the ambiguous genital or physical appearance?	**.65**	-.05	.27	.24
05b. How stressful is this to you?	**.67**	-.10	.34	.14
06a. Do people speak negatively about *you* because of your child?	**.76**	-.07	-.18	.13
06b. How stressful is this to you?	**.73**	-.11	-.17	.15
11a. Is your child called names or teased by other children because of child's ambiguous genital or physical appearance?	**.40**	.03	.24	.55
11b. How stressful is this to you?	**.41**	.02	.44	.49
03a. Can other people see that your child has an ambiguous appearance?	-.09	**.76**	.07	.35
03b. How stressful is this to you?	-.14	**.52**	.18	.48
04a. Do you think that other people look at your child because of the ambiguous appearance?	.39	**.67**	-.21	.16
04b. How stressful is this to you?	.17	**.57**	.13	-.01
07a. Does your child show more cross gender role behavior compared to other children? For parents of daughters: Does your daughter prefers more masculine activities than other girls? For parents of sons: does your son prefers more feminine activities compared to other boys?	-.06	**.87**	.10	.20
07b. How stressful is this to you?	-.01	**.91**	.04	.02
08a. Do other people speak or behave negatively about your child because of child's ambiguous behavior? (Daughters: masculine behavior and interests?; Sons: feminine behavior and interests?)	.11	**.44**	-.08	-.05
09a. Do other people isolate or reject *your child* because of ambiguous genital/physical appearance?	-.03	.34	**.76**	.19
09b. How stressful is this to you?	.04	.24	**.85**	.03
10a. Do other people isolate or reject *you* because of your child?	.17	-.10	**.86**	-.13
10b. How stressful is this to you?	.21	-.12	**.82**	-.14
12a. Is your child isolated or rejected by other children because of the ambiguous genital or physical appearance?	-.09	.00	**.75**	.45
12b. How stressful is this to you?	.02	-.08	**.88**	.22
13a. Does your child suffer from emotional problems because of the ambiguous genital or physical appearance?	.26	.00	-.07	**.75**
13b. How stressful is this to you?	.13	.02	-.03	**.82**
13c. How frequent was your child sad?	.09	.06	-.05	**.55**
13d. How frequent was your child depressed?	.01	-.01	.07	**.82**
13g. How frequent was your child shy?	-.14	.14	.13	**.71**
13h. How frequent was your child socially withdrawn?	-.11	.34	.13	**.61**
13e. How frequent was your child angry?	.01	.19	.20	.37
13f. How frequent was your child aggressive?	.12	.05	.28	.24
14. Are you worried about your child's future?	.20	-.01	.05	.29
15. Is it difficult for you to accept your child?	.25	.07	.02	-.12

[a] Stigmatization due to genital ambiguity and stress evoked by such experiences (α = .86).
[b] Stigmatization due to ambiguous body appearance or displayed ambiguous behavior and stress evoked by such experiences (α = .84).
[c] Social rejection or isolation due to DSD and stress evoked by being rejected or isolated (α = .88).
[d] Reported emotional problems seen in the child and parental stress evoked these emotional problems (α = .85).

Table 3b Factor loadings after varimax rotation and Cronbach's alphas of the SSS-DSD Adult report (N = 34)

Questions	Components		
	Verbal[a]	Behavior[b]	Emotion[c]
1a. Can other people see that you got a genital that is (slightly) different from that of other men/women?	**.63**	.03	.10
1b. How stressful is this to you?	**.62**	.36	.42
2a. Do you think that other people look at you because of the ambiguous genital?	**.79**	.33	.22
2b. How stressful is this to you?	**.86**	.19	.23
4a. Do you think that other people look at you because of the ambiguous appearance?	**.71**	-.08	.37
4b. How stressful is this to you?	**.82**	.21	.25
5a. Do other people speak negatively about you because of the ambiguous genital or physical appearance?	**.75**	.08	-.13
5b. How stressful is this to you?	**.86**	.10	-.05
7a. Do other people including family member speak or behave negatively about you because of you show more cross-gender behavior compared to others? (For woman: Do you prefer more masculine activities compared to other women? For man: do you prefer more feminine activities compared to other men?)	**.73**	-.27	.12
7b. How stressful is this to you?	**.71**	-.23	.12
3a. Can other people see that you have an ambiguous appearance?	.08	**.65**	.41
3b. How stressful is this to you?	.43	**.55**	.23
6a. Do you behave differently from other men/women?	.01	**.64**	.17
6b. How stressful is this to you?	.16	.36	.10
9a. Do other people teased you or called you by funny names because of the ambiguous genital or physical appearance?	.10	**.84**	.07
9b. How stressful is this to you?	.15	**.87**	.18
10a. Do other people isolate/reject you because of the ambiguous genital or physical appearance?	-.21	**.68**	.23
10b. How stressful is this to you?	-.21	**.68**	.23
13a. Do you suffer from emotional problems because of the ambiguous genital/appearance?	.31	.40	**.75**
13b. How stressful is this to you?	.31	.37	**.75**
13c. How frequently you were sad?	-.06	.20	**.94**
13d. How frequently you were depressed?	.11	.16	**.93**
13e. How frequently you were angry?	.34	.31	**.68**
13g. How frequently you were shy?	.17	.16	**.73**
13h. How frequently you were socially withdrawn?	.11	.14	**.71**
14. Are you worried about your future?	.21	.10	**.74**
15. Is it difficult for you to accept your condition?	-.02	.20	**.75**

[a] Verbal reaction received due to DSD conditions and the stress evoked by such experiences (α = .92).
[b] Behavioral reaction received due to DSD conditions and the stress evoked by such experiences (α = .85).
[c] Reported emotional problem due to having DSD conditions (α = .94).

Subgroup analysis

Table 4a and 4b summarize the comparisons of subgroups across gender, treatment status, gender change history, and visibility of DSD conditions from parent and adult report, respectively. In either boys or girls, children and adolescents experienced some degree of stigmatization. Particularly girls suffered more stigmatization due to ambiguous appearance or behavior and had more emotional problems than boys (see Table 4a; gender comparison). Women experienced more stigmatization and had more emotional problems than men. Both men and women experienced some degree of verbal and behavioral reactions due to their DSD conditions (see Table 4b; gender comparison).

Regardless of having received prior medical/surgical treatment for DSD, children and adolescents experienced stigmatization and had emotional problems (see Table 4a; treatment status comparison). However, untreated adults experienced more stigmatization than treated adults (see Table 4b; treatment status comparison).

Six youngsters and 15 adults were assigned female at birth and had a history of social gender role change. These patients experienced more stigmatization than patients who kept the gender assigned at birth. Particularly young patients experienced more stigmatization due to ambiguous appearance or behavior and had more emotional problem than youngsters who kept in the gender assigned at birth (see Table 4a; gender change history comparison). Adults experienced more behavioral stigmatization than adults who kept the gender assigned at birth (see Table 4b; gender change history comparison).

Children and adolescents with visible body ambiguity experienced stigmatizations more frequently than patients who could conceal ambiguous characteristics (see Table 4a; visibility of DSD comparison). Regardless of the visibility of their DSD conditions, Children and adolescents reported emotional problems due to DSD. Adults with visible body ambiguity experienced more stigmatization than adults who could conceal ambiguous characteristics; this was particularly seen in verbal and behavioral stigmatization (see Table 4b; visibility of DSD comparison).

Table 4a Median domain and overall sumscores of the SS-DSD Parent-Report across gender, treatment status, gender change history, and visibility of DSD

SS-DSD Parent-Report	Gender			Treatment status			Gender change history			Visibility of DSD		
	Boys (*n* = 57)	Girls (*n* = 24)	*p*	Treated (*n* = 54)	Untreated (*n* = 27)	*p*	Yes (*n* = 6)	No (*n* = 75)	*p*	Visible (*n* = 12)	Concealable [a] (*n* = 69)	*p*
Genital ambiguity	12 (10-50)	10 (10-27)	.48	11 (10-50)	15 (10-37)	.20	16 (10-23)	12 (10-50)	.26	18 (10-32)	11 (10-50)	**.006**
Behavior ambiguity	10 (10-14)	10 (10-30)	**<.001**	10 (10-23)	10 (10-30)	.42	11 (10-30)	10 (10-23)	**.01**	14 (10-30)	10 (10-21)	**<.001**
Rejection	10 (10-37)	10 (10-23)	.26	10 (10-37)	10 (10)	.14	10 (10)	10 (10-37)	.99	10 (10-37)	10 (10-22)	**.01**
Emotional problems	10 (10-28)	10 (10-32)	**.002**	10 (10-32)	10 (10-22)	.44	14 (10-22)	10 (10-32)	**.02**	10 (10-32)	10 (10-32)	.11
Total score [b]	43 (40-103)	49 (40-98)	.23	43 (40-103)	45 (40-74)	.47	54 (45-74)	42 (40-103)	**.02**	61 (40-98)	42 (40-103)	**.002**

Note. Data were presented as median (range). The Mann-Whitney U test was applied.to obtain p-values

[a] Concealable DSD condition comprised both partly hidden and hidden types of DSD condition

[b] Unweighted sum score

Table 4b Median domain and overall sumscores of the SSS-DSD Adult-Report across gender, treatment status, gender change history, and visibility of DSD

Scale	Gender			Treatment status			Gender change history			Visibility of DSD		
	Men (*n* = 20)	Women (*n* = 14)	*p*	Treated (*n* = 15)	Untreated (*n* = 19)	*p*	Yes (*n* = 15)	No (*n* = 19)	*p*	Visible (*n* = 17)	Concealable[a] (*n* = 17)	*p*
Verbal stigmatization	12 (10-47)	10 (10-28)	.78	10 (10-36)	14 (10-47)	.14	14 (10-47)	10 (10-28)	.11	15 (10-47)	10 (10-21)	**.015**
Behavioral stigmatization	10 (10-26)	11 (10-37)	.30	10 (10-23)	10 (10-37)	.25	11 (10-31)	10 (10-37)	**.03**	13 (10-37)	10 (10-11)	**.001**
Emotional problems	14 (10-40)	29 (10-47)	**.009**	12 (10-40)	21 (10-47)	.07	16 (10-47)	10 (10-44)	.52	16 (10-47)	16 (10-40)	.60
Total score [b]	37 (30-91)	50 (31-100)	**.042**	36 (30-83)	48 (31-100)	**.046**	41 (31-100)	38 (30-97)	.80	46 (31-100)	38 (30-63)	.19

Note. Data were presented as median (range). The Mann-Whitney U test was applied to obtain p-values

[a] Concealable DSD condition comprises partly hidden and hidden type of DSD conditions

[b] Unweighted sum score

Qualitative analysis

The codes that emerged from the data were clustered into five broader themes; they are presented in table 5. Relationships between themes were investigated and significant overlaps between themes were found. 'Knowledge' is associated with all themes, 'person' and 'society' are associated with responses, and 'person's response' is associated with 'society's response towards DSD'.

Table 5 Themes, codes, number of references coded, and quotes obtained from the qualitative data

Themes	Description	Number of references coded	Quotes
Knowledge on DSD	All existing knowledge, information, ideas, myths, beliefs either correct or incorrect	169	"Neighbors or relatives often asked "why do you have a male voice?" "People believed that our child and our family were cursed or got bad karma… they said "how come a girl has a penis?" "When I was in high school, my classmates recognized that my breasts were bigger than other boys in comparison; I was confused, don't know how that could have happened." "Our neighbor often invited me to visit and play with their children, but I was afraid I wouldn't be able to answer them should they have questions."
Patient's factors	Refers to personal characteristics, emotions, concept of being different, and DSD characteristics	411	"She has had a few friends since childhood, now she seems to have lack of self-confidence. Her friends also rarely asked to play with her." "As I used to be tomboy since childhood. I don't care what people say about me. As an athlete, it's common to have a well-built body." "Sometimes I feel hopeless and helpless because I don't have friends to talk with about my condition."
Patient's response	Patient's responses to society and behaviors related to coping with DSD	54	"I don't know what to do; so I'd better do nothing." "My friend supported me and told me that I should go to a doctor, so I went to hospital." "I got a job before graduated from college. My supervisor supported me. I told her about my condition and she allowed me to take a day off so I could go for treatment." "When I was in *SMP* (school level for teen aged 14), some classmates were gossiping about me; they said that I was similar to a *'bencong'* or *'waria'* on the TV. I couldn't stand to hear that, so I quit from school.I"
Social factors	Refers to all social factors such as demographics, norms, expectancies, activities	208	"All people in our village know about my child's condition.." "We don't have money; we are only able to come for treatments when we get supports from others (neighbors, employer)." "My husband could divorce me if I told him that I could not have a child." "I want to marry my girlfriend but I am afraid she can't accept the fact that I can't give her a child." "I felt my parents don't care about me, because when I asked them to visit a doctor, they asked me to wait." "Will he be able to (sexually) satisfy his wife in the future? If he can't get married, we will be ashamed and very disappointed."

(continued)

Table 5 Themes, codes, number of references coded, and quotes obtained from the qualitative data *(continued)*

Themes	Description	Number of references coded	Quotes
Society's response	All actions and behaviors towards patients with DSD and their parents	102	"When the baby was born, people were shocked and gossiping." "People often asked me seriously or just as a joke… is your child actually a boy or a girl?" "Her classmates often called her *'banci'*.. also her friends in *'pengajian'* did the same.. so she quit from *'pengajian'*. "People know about my child's condition; his friends called him *'banci'* and it made him cry. Although my child showed his genitals to proof that he has a penis, they keep on teasing him like that."

Note. 'Banci, waria' (in Indonesian language), or *'bencong, wandu'* (in Javanese language) refer to transgender
'Pengajian' is an informal course for reading Koran or Arabic language.

Discussion

In this study we performed a systematic exploration of Indonesian patients' and parents' experiences with stigmatization due to DSD. Present clinical management includes surgical and hormonal treatments to prevent stigmatization and to facilitate social participation.[1] However, the stigmatization itself has never been studied systematically. As almost all parents living in western countries choose such treatments, it is difficult to study potential social stigmatization in DSD patients. and how stressful it was for them. Our study presents a comprehensive overview about the types of stigmatization on persons with DSD, the socio-cultural context related to the stigmatization that may explain why such experience is more stressful for particular groups of patients but not or less stressful to others. Analysis on psychometric properties revealed that using the SSS-DSD Parental version, we were able to measure stigmatization in four domains: genital ambiguity and evoked stress, ambiguous body appearance or displayed ambiguous behavior and evoked stress, social rejection or isolation and evoked stress and children's emotional problems parental evoked stress. On the SSS-DSD patient version we revealed three domains: received verbal reactions and evoked stress; received behavioral reactions and evoked stress; and emotional problems.

Further analysis showed that patients with DSD experienced stigmatization due to their DSD condition. Patients with an ambiguous body and females reported experienced stigmatization more frequently than patients who could hide their body ambiguities. Moreover, stigmatization is also prominent among patients with a history of social gender role change and in untreated adult patients. It is obvious the more frequent patients reported experiences of stigmatization, the higher the stress evoked by these experiences.

We identified five themes related to stigmatization and stress reported by patients and parents: lack of knowledge about DSD, patient-related factors, society-related factors, patient's response towards the environment, and society's response towards patients with DSD. These five themes play an important role in the stigmatization on patients with DSD (see Table 5). Ambiguity in body, genitals, or gender role behavior due to a DSD condition is obvious to laymen but these were not understood well among patients and their society. The general population of Indonesia considers a mix up DSD and transgenderism. A hostile attitude towards those who show variance in gender is often met; patients are teased, humiliated and rejected (so called: in *Bahasa: 'waria'*; in *Javanese: 'bencong'* for transgender people). Recently, Moslem clerics in Indonesia banned gender reassignment surgery and also all parties involved, such as medical doctors, judges. [13] This makes patients and parents of youngsters with a visible DSD condition were more stressful than those who have concealable DSD condition. Patients with a visible DSD condition cannot avoid society's response towards them, either passively (e.g. crying, or do nothing) or actively (e.g. seek advice, disclose to others). Patients with a concealable DSD condition, have more possibilities to hide their DSD (i.e. clothing) and can therefore mitigate or even avoid society's unexpected or unwanted response. However, it is important to emphasize that patients with concealable DSD condition do not report less emotional problem than patients who have visible DSD condition. Whether DSD condition was known by others or not, having a DSD condition is problematic and hard to cope for patients.

Living in the Indonesian society that highly values procreation and progeny makes patients and parents worry about infertility and possibility of marriage in the future.[14-15] Among women, concern about risk of being divorced due to infertility was addressed by patients as well as parents. Our finding are in line with previous studies reporting sexual distress, disclosure dilemmas, and tendency to avoid romantic relationships among women with DSD, and

similar concern on infertility and fear of rejection from potential partner among adults with DSD.[16] Although Indonesia is not classified as a masculine society, women seem more often in the vulnerable position in the society. A previous study reported that 15 Indonesian adults with DSD who underwent a female-to-male social gender change experienced gender dysphoria during their living as women, but not during their living as men.[17] Our study demonstrated that young girls and adult women experienced more stigmatization than young boys or adult men. Education about DSD should be designed to promote self-empowerment for patients with DSD, particularly for young girls and adult women with DSD.

In conclusion, the majority of patients in this study experienced stigmatization due to their DSD condition. The more frequent stigmatization was experienced, the higher their stress level. Patients who anticipated stigmatization reported emotional problems as well as patients who experienced social stigmatization. Having a visible DSD characteristic, female, and living in rural areas are identified as risk factors for stigmatization due to DSD in Indonesia. Limited knowledge about DSD may be barrier for acceptance towards DSD and patients with DSD. Education about DSD and how to cope with it should also be designed by considering the socio-cultural context and should be made accessible for patients and laymen.

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Chapter 7

Health-related quality of life in Indonesian children, adolescents, and adults with disorders of sex development

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Abstract

Background. Patients with a disorder of sex development (DSD) have ambiguous primary sex characteristics and will develop ambiguous secondary sex characteristics if left untreated. Life can be difficult for persons with DSD as they have to live with an ambiguous appearance. It can raise confusion about one's gender and stigma on body ambiguity may lead to unpleasant social reactions. In this study we investigated the impact of DSD on patients' quality of life.
Purpose. To assess health-related quality of life in Indonesian patients with DSD, who received limited or no medical treatment for most of their life.
Method. 118 patients born with DSD, aged 6-41 years (60 children, 24 adolescents, 34 adults) were compared to 118 healthy control subjects matched for gender, age, and residential setting. The Indonesian versions of TACQOL PF, TACQOL CF, and TAAQOL were used. The psychometric properties of these measures are reported here.
Results. Compared to parents of matched control children, parents of children with DSD reported more problems in social functioning and stated their children were less happy. Adult patients reported more depression than matched controls adults. No differences were found between patients and matched control in adolescents sample, either based on parental or adolescent self-reports.
Conclusion. We observed that social and emotional functioning of Indonesian patients with DSD was affected. Psychological assessment and interventions on coping should be integrated in the medical treatment. Early identification of DSD is crucial to prevent worsening of psychological problems.

Keywords: disorders of sex development, health-related quality of life, late identified, Indonesia

Background

Disorders of Sex Development (DSD) is a group of congenital anomalies as a result of which patients are characterized by genital, body and psychological ambiguity [1]. The physical appearance and psychological make-up may have both male and female sex characteristics. In addition, most patients are infertile. The origins of their genital, body and psychological ambiguity are abnormalities in anatomic development and hormonal disturbances. In most cases, patients with DSD do not suffer from physical impairment, but the ambiguity of their bodies and minds may make life difficult. Subsequently they impact their quality of life (QoL) as such ambiguities are rarely seen and not understood by patients themselves, or their parents, neither by members of their community. Health-related quality of life (HRQoL) has been used as an outcome measure to assess the influence of disease and treatment in daily life by considering both health status and negative emotions that by the limitations in the health status.

Wisniewski and coworkers reviewed 35 studies published between 1955 and 2009 on QoL among females with 46,XY karyotypes or born with ambiguous genitalia due to androgen insensitivity syndrome, 5alpha-reductase-2deficiency, or 17beta-hydroxysteroid dehydrogenase deficiency [2]. They found that more studies had been conducted on women with complete androgen insensitivity syndrome (CAIS) than other diagnoses during that period. Although it was observed that adults with partial androgen insensitivity syndrome (PAIS), regardless of female or male rearing, experienced severe problem with mental health, not all studies could provide supporting evidence. Moreover, studies that reported better QoL of patients than healthy control subjects were often performed on a small sample [2]. In a recent study by Kleinemeier and colleagues, 54 adolescent German girls aged 13-16 with different types of DSD reported a better QoL compared to their national reference group, but six boys with DSD did not [3].

Fagerholm and coworkers assessed HRQoL in 16 women with 46,XX congenital adrenal hyperplasia (CAH) and 8 women with AIS who had undergone genital surgeries in childhood and observed a good QoL in fact similar to the general population[4]. Recently, Zainuddin and colleagues reviewed 12 QoL studies on patients with 46,XX CAH reported from 7 Western countries and two Asian countries (Malaysia and Vietnam). They observed that some studies reported no difference between 46, XX CAH patients and the comparative

groups, but other studies reported improvement or worsening of QoL. This report also highlights factors that may influence QoL of patients living in developing countries (India, Vietnam, Malaysia), such as delayed diagnoses due to lack of expertise, financial constraints, or cultural bias towards the male gender[5]. Despite extensive number of studies, factors impacting QoL in patients with DSD remain inconclusive.

In Western countries, the majority of patients will be referred to specialized centers for diagnostics and treatment soon after identification mostly in the newborn age period. In Indonesia, DSD is largely unknown, even among health practitioners. As a consequence, DSD is often identified late, diagnostic procedures are delayed or not performed and many patients never receive any medical treatment. These patients have doubts about their gender as they have to live with ambiguous genitalia, and, from adolescence onwards, with bodies with both male and female characteristics. Moreover, in a country where people value progeny highly and expect everyone to get married and become parents, infertility can be a major issue. As the majority of studies performed in Western countries was conducted among patients who had received medical treatment early in life, the findings cannot easily be applied in Indonesian patients as there are great difference in medical and cultural context.

Our study aims to investigate the HRQOL in Indonesian children, adolescents, and adult patients with DSD who only had received little medical attention and treatments or no medical treatments at all in comparison to healthy matched control subjects.

Outline of the report

We report our studies in two parts. First, we report the scale adaptation, pilot study, validity and reliability studies of the selected HRQoL measures. Subsequently we report outcomes on HRQoL in Indonesian children, adolescents, and adults with DSD.

Method

This cross-sectional study was part of large psychological study that was conducted jointly with a clinical study on the etiology of DSD in Semarang, Indonesia [6]. The study protocol was approved by the board of the ethical committee from the Faculty of Medicine, Diponegoro University, Semarang, Indonesia.

Scale adaptation and pilot study for assessment of HRQoL

Prior to this study, there were no relevant measure for HRQoL was available in the local language (*Bahasa Indonesia*). Therefore we used a measure developed in Western countries that had been applied many times in comparable studies across different nations (TAQCQOL/TAAQOL) [7-9].

Method

The scale adaptation was conducted through the following stages: translation into local language (*Bahasa Indonesia*) by a certified translator, panel review on the Indonesian translations of the measures by involving local researchers and an anthropologist who had vast expertise in Indonesian culture and understood both Dutch and Indonesian languages, and a pilot study involving healthy subjects and patients with DSD to evaluate the applicability of the measures. To assess validity and reliability in measures applied in children and adolescents, data were obtained from healthy participants contacted via schools.

Participants

Pilot study participants. Thirty-six subjects, aged 6-25 years, male or female, were recruited for the pilot study group, which comprised six patients (two adults, two adolescents, two children) and 30 healthy subjects (10 children, 10 adolescents, 10 adults). The healthy subjects, from different socioeconomic backgrounds, were contacted through the local leaders (*Pak RT*) and joined the study voluntarily. Oral and written study information was given by the researcher (AE). After the adult participants and parents of subjects under age 18 had given their consent, questionnaires were administered in a similar procedure for patients and matched controls to study the applicability of the initial protocol. The participants received a gift (stationery or towel) in thanks for their participation.

Psychometric study participants. To assess the validity and reliability of the measures, data were obtained from 672 healthy subjects: 216 children aged 8-11; 68 adolescents aged 12-15, 57 parents of children aged 6-15, and 326 adults aged 16-34. The participants was mostly females (58.6%) ,were Javanese in ethnicity (92%), and Moslem (93.5%). They were recruited from five schools and three universities in the Central Java region (Semarang, Pekalongan, Yogyakarta, and Solo). Data of TACQOL PF 6-11 were obtained from 57 parents

of elementary school students during the regular parent meeting held by the school.

Measures

A generic measure of HRQoL was chosen: the TNO-AZL Children Quality of Life Questionnaire Parent Form (TACQOL-PF)[7], the TNO-AZL Children Quality of Life Questionnaire Child Form (TACQOL-CF)[8], and the TNO-AZL Adult Quality of Life Questionnaire (TAAQOL)[9]. The TACQOL / TAAQOL assesses the frequency of problems (range from "never" to "often" on a 5-point scale) and how subject feels about having this problem (ranged from "bad" to "alright"; scored 0 to 4). The scores in each 8-item scales ranged from 0 to 32; the 8-item scales for positive or negative moods ranged from 0 to 16, in total. In all scales, higher scores indicated a higher QoL. We decided to select scales relevant to assess the impact of DSD in the patient's life. We excluded scales on motor functioning and physical pain (TAAQOL) as impairments in motor functioning and physical pain are not seen in patients with DSD .

TACQOL-PF is developed for assessing HRQoL in children aged 6 to15 years. The parent is the informant[10]. In this study, we applied four scales: Cognition (8 items assessing problems with cognitive functioning and school performance), Social (8 items assessing problems in social functioning with parents and peers), Positive Emotion (8 items assessing the occurrence of positive moods), and Negative Emotion (8 items assessing the occurrence of negative moods).

TACQOL-CF is a self-report instrument for children aged 8 to15 years assessing the true proxy. The TACQOL-CF 8-11 comprised similar scales of TACQOL-PF 6-11[10] and we applied the same four scales as applied in TACQOL PF: Cognition, Social, Positive and Negative Emotions . For the TACQOL-CF 12-15, we selected the scales relevant for this study: Cognition (8 items), Peers (4 items assessing problems in social functioning with peers), Positive emotion (8 items), and Negative emotion (8 items)[11].

TAAQOL is a self-report instrument assessing HRQoL for subjects aged 16 years or older[12]. We applied nine relevant scales: Cognition (4 items), Sleep (4 items assessing sleep problems), Social (4 items), Daily Activities (4 items assessing limitation in independent daily functioning), Sex (2 items assessing sex-related problems), Vitality (4 items assessing the occurrence of feelings of vitality), Happiness (4 items assessing the occurrence of positive mood),

Depressive Mood (4 items assessing the occurrence of depressive mood), and Anger (3 items assessing the occurrence of angry mood)[12].

Statistical analysis

We followed the procedures for assessing psychometric properties described in the original versions of measures [10-12]. Prior to analysis, raw scores were transformed into the weighted scores. Construct validity was explored using principal component analysis (PCA) with varimax rotation method and Kaiser normalization. Item-total correlation was analyzed using the Pearson's product moment test. We evaluated the reliability of instruments using the internal consistency with Cronbach's alpha as the outcome measures.

Results

During the pilot testing, we learned that participants were willing to discuss questions related to QoL, but the paper-and-pencil methods was only effective for educated participants who were familiar with self-report measures. For participants with limited education or were illiterate and participants who were unfamiliar with self-reports, oral application of the measure was the best approach to apply measures. Oral application ensured participants understood the questions before they gave an answer. We asked parents and patients to give an answer according to the pre-set response categories in the questionnaire, similar to parents who filled out the paper-and-pencil questionnaire had to do.

TACQOL PF 6-15

The PCA generated two components of Cognition and Social scales that explained 42.2% of the total variance, and two components of Positive and Negative emotion scales that explained 44.5% of the total variance. Table 1a shows the factor loading after varimax rotation on the four scales. Three items (Cognition 8, Social 7, Positive emotion 4) did not loaded to the expected components, and five items had factor loadings <.40. Table 1b shows the item-total correlation coefficients and the obtained Cronbach's alphas (ranged between α = .53 and α = .87; original manual: between α = .67 and α = .84). Despite of the PCA results, only one item (Positive emotion 4) violated the assumption that the corrected item-total correlation coefficient should be higher than the remaining item-scale correlation coefficients.

Table 1.a. Factor loadings after varimax rotation on data of the TACQOL PF 6-15 (n = 57)

Items	Cognition	Social	Items	Positive emotion	Negative emotion
Cognition 1	**.67**	.12	Positive emotion 1	-.36	**.64**
Cognition 2	**.79**	.15	Positive emotion 2	-.67	**.53**
Cognition 3	**.78**	.07	Positive emotion 3	-.41	**.42**
Cognition 4	**.67**	-.004	Positive emotion 4	-.58	.14
Cognition 5	**.82**	.20	Positive emotion 5	-.18	**.68**
Cognition 6	**.77**	-.05	Positive emotion 6	-.55	**.65**
Cognition 7	**.74**	.09	Positive emotion 7	.05	**.62**
Cognition 8	.28	**.57**	Positive emotion 8	-.45	**.67**
Social 1	.19	.24	Negative emotion 1	**.71**	-.26
Social 2	.24	.37	Negative emotion 2	**.66**	-.10
Social 3	.02	**.75**	Negative emotion 3	.01	-.29
Social 4	.04	**.53**	Negative emotion 4	**.69**	-.37
Social 5	-.23	**.54**	Negative emotion 5	**.41**	.20
Social 6	.32	**.61**	Negative emotion 6	**.58**	.11
Social 7	**.46**	.07	Negative emotion 7	**.41**	**.55**
Social 8	-.05	.38	Negative emotion 8	.31	-.17

Note. PCA was performed separately on item with the combined-score and items with single response measuring emotion and was instructed to extract 2 component in each analysis.

Table 1.b. Item-scale and corrected item-scale correlation coefficients and the Cronbach's alphas of TACQOL PF 6-15 scales ($n = 57$)

Item / Scales	Cognition	Social	Positive Emotion	Negative Emotion
Cognition 1	**.59**	-.21	-.47	-.28
Cognition 2	**.70**	-.38	-.53	-.55
Cognition 3	**.67**	-.31	-.43	-.34
Cognition 4	**.56**	-.14	-.16	-.29
Cognition 5	**.78**	-.29	-.47	-.44
Cognition 6	**.66**	-.16	-.31	-.44
Cognition 7	**.65**	-.26	-.44	-.32
Cognition 8	**.32**	-.33	-.14	-.26
Social 1	-.20	**.20**	-.25	-.22
Social 2	-.25	**.16**	-.40	-.02
Social 3	-.14	**.39**	-.24	-.18
Social 4	-.15	**.20**	-.32	-.24
Social 5	.11	**.31**	-.04	.01
Social 6	-.38	**.38**	-.16	-.13
Social 7	-.38	**.20**	-.19	-.13
Social 8	-.03	**.26**	.01	-.29
Positive emotion 1	.30	.25	**.63**	.30
Positive emotion 2	.49	.24	**.75**	.44
Positive emotion 3	.32	.18	**.50**	.39
Positive emotion 4	**.49**	.39	.37	.43
Positive emotion 5	.26	.26	**.55**	.24
Positive emotion 6	.34	.29	**.72**	.43
Positive emotion 7	.25	.08	**.38**	.11
Positive emotion 8	.38	.38	**.69**	.36
Negative emotion 1	-.44	-.33	-.51	**.50**
Negative emotion 2	-.39	-.18	-.41	**.43**
Negative emotion 3	-.06	-.05	-.16	**.14**
Negative emotion 4	-.48	-.27	-.63	**.42**
Negative emotion 5	-.25	-.19	-.13	**.24**
Negative emotion 6	-.25	-.29	-.22	**.37**
Negative emotion 7	-.11	.00	.10	**.20**
Negative emotion 8	-.20	-.02	-.27	**.27**
Cronbach's alpha (α)	.87	.53	.84	.61

TACQOL CF 8-11

Two components were extracted by PCA which explained 30.9% of the total variance and two components of Positive and Negative emotion scales that explained 31.3% of the total variance. Table 2a shows the factor loading after varimax rotation on the four scales. The item structure of cognitive and social scale violated the original structure; however, this was not observed in the emotion scales. Only one item in each emotion scales had factor loading <.40 (Positive emotion 7 and Negative emotion 5).

Table 2.a. Factor loadings after varimax rotation on data of the TACQOL CF 8-11 (n = 216)

Items	Cognition	Social
Cognition 1	**.52**	-.17
Cognition 2	.19	.02
Cognition 3	.13	.38
Cognition 4	**.56**	.18
Cognition 5	.06	**.63**
Cognition 6	.17	**.67**
Cognition 7	**.40**	.35
Cognition 8	.26	**.45**
Social 1	-.25	**.53**
Social 2	.39	.20
Social 3	-.08	**.61**
Social 4	.17	**.54**
Social 5	-.04	**.49**
Social 6	.28	.28
Social 7	**.65**	.08
Social 8	**.76**	-.12

Items	Positive emotion	Negative emotion
Positive emotion 1	**.69**	-.01
Positive emotion 2	**.46**	.08
Positive emotion 3	**.62**	-.08
Positive emotion 4	**.62**	-.16
Positive emotion 5	**.56**	.10
Positive emotion 6	**.41**	-.08
Positive emotion 7	.30	.04
Positive emotion 8	**.55**	-.24
Negative emotion 1	-.06	**.67**
Negative emotion 2	.01	**.56**
Negative emotion 3	-.19	**.56**
Negative emotion 4	-.11	**.53**
Negative emotion 5	.04	.08
Negative emotion 6	.22	**.48**
Negative emotion 7	-.05	**.62**
Negative emotion 8	-.24	**.64**

Table 2b shows the item-total correlation coefficients and the obtained Cronbach's alphas (ranged between α = .37 and α = .63). These Cronbach's alphas obtained were lower than the manual (ranged between α = .65 and α = .79). In contrast to the PCA results, corrected item-total scale correlations coefficients were higher than the remaining item-scale correlation coefficients, in all items.

Table 2.b. Item-scale and corrected item-scale correlation coefficients and the Cronbach's alphas of TACQOL CF 8-11 scales ($n = 216$)

Item pair	Cognition	Social	Positive Emotion	Negative Emotion
Cognition 1	**.16**	-.04	-.06	-.01
Cognition 2	**.14**	-.02	-.04	-.10
Cognition 3	**.24**	-.03	-.31	-.22
Cognition 4	**.37**	-.15	-.13	-.10
Cognition 5	**.27**	-.25	-.13	-.04
Cognition 6	**.35**	-.27	-.20	-.05
Cognition 7	**.27**	-.27	-.01	-.06
Cognition 8	**.29**	-.21	-.21	-.05
Social 1	-.10	**.15**	-.16	-.02
Social 2	-.19	**.32**	.01	-.03
Social 3	-.09	**.26**	-.22	-.07
Social 4	-.20	**.34**	-.13	-.13
Social 5	-.15	**.17**	-.16	-.15
Social 6	-.14	**.31**	-.05	-.14
Social 7	-.09	**.33**	.03	-.10
Social 8	-.13	**.26**	.03	-.25
Positive emotion 1	.14	.04	**.46**	-.01
Positive emotion 2	.17	.10	**.24**	.10
Positive emotion 3	.11	.06	**.41**	-.01
Positive emotion 4	.01	-.08	**.45**	.03
Positive emotion 5	.03	.13	**.34**	-.03
Positive emotion 6	.14	.03	**.27**	.19
Positive emotion 7	.16	.07	**.18**	.12
Positive emotion 8	.24	.13	**.38**	.11
Negative emotion 1	-.10	-.11	-.12	**.35**
Negative emotion 2	-.04	-.08	-.16	**.20**
Negative emotion 3	.02	.01	-.02	**.15**
Negative emotion 4	.17	-,16	-.11	**.26**
Negative emotion 5	-.03	-.02	-.04	**.05**
Negative emotion 6	-.16	-.22	-.08	**.28**
Negative emotion 7	-.03	-.13	.08	**.30**
Negative emotion 8	-.15	-.15	-.21	**.36**
Cronbach's alpha (α)	.47	.55	.37	.63

TACQOL CF 12-15

For the TACQOL CF 12-15, PCA generated two components of Cognition and Peers which explained 43.5% of the total variance and two components of Positive and Negative emotion scales that explained 35.4% of the total variance. Table 3a shows the factor loading after varimax rotation on four scales. The results show two problematic items that loaded onto different component (Cognition 8 and Peer 2), and three items of emotion scales had factor loading <.40 (Positive emotion 2, Positive emotion 6, and Negative emotion 4).

Table 3.a. Factor loadings after varimax rotation on data of the TACQOL CF 12-15 (n = 68)

Items	Cognition	Social
Cognition 1	**.71**	-.23
Cognition 2	**.73**	.15
Cognition 3	**.61**	.20
Cognition 4	**.57**	.25
Cognition 5	**.38**	.42
Cognition 6	**.17**	.59
Cognition 7	**.73**	.11
Cognition 8	.28	**.79**
Peer 1	-.17	**.64**
Peer 2	**.50**	.24
Peer 3	.13	**.42**
Peer 4	.14	**.63**

Items	Positive emotion	Negative emotion
Positive emotion 1	**.76**	-.22
Positive emotion 2	.35	.10
Positive emotion 3	**.74**	.04
Positive emotion 4	**.83**	-.07
Positive emotion 5	**.23**	-.21
Positive emotion 6	.17	-.05
Positive emotion 7	**.47**	.19
Positive emotion 8	**.86**	-.06
Negative emotion 1	-.16	**.67**
Negative emotion 2	.15	**.48**
Negative emotion 3	-.08	**.40**
Negative emotion 4	-.29	.21
Negative emotion 5	-.04	**.51**
Negative emotion 6	-.46	**.41**
Negative emotion 7	-.02	**.60**
Negative emotion 8	.03	**.73**

Table 3b shows the item-total correlation coefficients and the obtained Cronbach's alphas (ranged between α = .27 and α = .81). Two items of Positive Emotion scale violated the assumption that the corrected item-total scale correlation coefficient should be higher than the remaining item-scale correlation coefficients (Positive emotion 6 and Positive emotion 7). These Cronbach's alphas obtained were lower than the manual, except in Negative Emotion scale (α = .81) that has higher alpha than the manual (α = .76).

Table 3.b. Item-scale and corrected item-scale correlation coefficients and the Cronbach's alphas of TACQOL CF 12-15 scales (n = 68)

Item / Scales	Cognition	Social	Positive Emotion	Negative Emotion
Cognition 1	**.36**	-.10	-.05	-.31
Cognition 2	**.59**	-.25	-.08	-.39
Cognition 3	**.50**	-.28	-.20	-.36
Cognition 4	**.43**	-.33	.20	-.24
Cognition 5	**.46**	-.16	-.03	-.25
Cognition 6	**.34**	-.24	-.14	-.19
Cognition 7	**.55**	-.31	-.02	-.23
Cognition 8	**.47**	-.46	-.09	-.32
Peer 1	-.10	**.35**	-.11	-.31
Peer 2	-.38	**.24**	-.16	-.40
Peer 3	-.12	**.29**	-.01	-.13
Peer 4	-.31	**.32**	-.12	-.29
Positive emotion 1	.20	.25	**.39**	.34
Positive emotion 2	-.01	.16	**.21**	.15
Positive emotion 3	.30	.12	**.34**	.18
Positive emotion 4	.10	-.06	**.38**	-.001
Positive emotion 5	.01	-.06	**.05**	-.04
(Positive emotion 6)	.10	.16	**(.08)**	.17
Positive emotion 7	-.01	.11	**.06**	.09
Positive emotion 8	.15	.13	**.43**	.22
Negative emotion 1	-.42	-.34	-.07	**.42**
Negative emotion 2	-.14	-.24	.05	**.31**
Negative emotion 3	-.27	-.23	-.05	**.24**
Negative emotion 4	.06	-.09	-.24	**.38**
Negative emotion 5	-.39	-.35	-.07	**.25**
Negative emotion 6	-.19	-.05	-.27	**.21**
Negative emotion 7	-.36	-.51	.05	**.30**
Negative emotion 8	-.45	-.27	-.14	**.44**
Cronbach's alpha (α)	.75	.49	.27	.81

TAAQOL

For the TAAQOL, the PCA generated nine components with 63.1% of the total variance was explained. Factor loadings after varimax rotation are presented in Table 4a. Items assessing cognitive functioning, sleep problem, sexual functioning, and happiness are loaded well onto the expected components. In the remaining scales, there are one or two items that not loaded onto the expected components, but only one item (Social 1) had factor loading <.40.

Table 4.a. Factor loadings after varimax rotation on data of the TAAQOL (n = 326)

Item/scales	Cog-nition	Sleep	Social	Daily	Sex	Vital-ity	Happi-ness	Depres-sive	An-ger
Cognition 1	**.61**	.08	.22	-.12	.23	-.08	-.05	-.15	.06
Cognition 2	**.73**	.00	.04	.14	-.03	-.23	.02	.00	.06
Cognition 3	**.75**	-.01	-.16	-.19	.00	.01	.11	-.12	.00
Cognition 4	**.59**	.21	-.15	-.08	-.02	.23	-.07	.05	-.10
Sleep 1	.17	**.70**	.28	-.12	-.10	.09	-.09	-.15	.07
Sleep 2	.09	**.82**	-.07	-.03	-.08	.02	.14	.25	.15
Sleep 3	.10	**.71**	.05	.00	.15	.07	.03	-.05	.07
Sleep 4	.11	**.86**	-.08	.06	-.07	.06	.10	.16	-.02
Social 1	.17	.26	.10	-.69	-.03	.07	.00	.00	-.02
Social 2	.26	.10	**.65**	-.42	-.08	.04	.07	.14	.05
Social 3	.01	-.08	.32	.03	-.28	-.32	.20	**.34**	-.16
Social 4	.00	.04	**.78**	.14	-.05	.01	.16	-.06	.19
Daily 1	**.65**	.16	.21	.10	-.06	.18	.05	.01	.18
Daily 2	.35	.20	.16	**.44**	-.03	.04	.02	.37	-.01
Daily 3	**.63**	.19	.09	.19	-.05	.33	-.02	.11	.01
Daily 4	.35	.26	.09	**.56**	-.06	.13	.10	-.03	.06
Sex 1	.00	.03	-.06	.02	**.86**	.00	-.04	.03	.02
Sex 2	.03	-.08	-.05	-.02	**.85**	-.11	-.08	.12	.03
Vitality 1	.17	-.05	-.17	-.16	-.14	.04	**.69**	-.04	.08
Vitality 2	.03	.11	.00	.13	-.07	**.76**	-.02	-.18	.25
Vitality 3	.19	-.02	-.09	.06	-.19	.19	**.57**	-.38	.16
Vitality 4	.13	.16	-.03	-.06	-.26	**.68**	.24	.12	.12
Happiness 1	-.06	-.03	.14	.12	.00	.02	**.76**	.06	.03
Happiness 2	-.01	.08	.07	.00	-.04	-.08	**.87**	.02	.05
Happiness 3	-.04	.12	.07	.08	.00	-.02	**.85**	.07	.03
Happiness 4	-.04	.06	.12	-.03	.04	.03	**.81**	.02	.08
Depressive 1	.17	.14	-.16	-.01	-.11	-.05	.07	.07	**.65**
Depressive 2	-.21	.15	-.07	.09	.27	-.01	.04	**.66**	.14
Depressive 3	.05	.13	.12	.05	-.08	.22	.25	.21	**.60**
Depressive 4	.13	.13	.00	-.18	-.18	.29	.01	**.52**	.45
Anger 1	.04	-.06	.11	-.07	.17	.12	.06	-.02	**.78**
Anger 2	.04	-.05	.10	-.09	.23	**.47**	-.11	.33	-.05
Anger 3	-.11	.05	.20	.13	.10	.06	.03	-.06	**.75**

Table 4b displays the item-total correlation coefficients and the Cronbach's alphas obtained (ranged between α =.34 and α =.86). In contrast to the PCA results, corrected item-total scale correlations coefficients were higher than the remaining item-scale correlation coefficients , in all items.

Table 4.b. Item-scale and corrected item-scale correlation coefficients of TAAQOL scales (n = 326)

Item/scales	Cog-nition	Sleep	Social	Daily	Sex	Vital-ity	Hap-piness	Depres-sive	An-ger
Cognition 1	**.47**	-.26	-.13	-.42	-.11	-.15	-.09	-.14	-.17
Cognition 2	**.49**	-.22	-.12	-.50	.01	-.18	-.01	-.21	-.16
Cognition 3	**.67**	-.26	-.16	-.46	.02	-.30	-.11	-.18	-.12
Cognition 4	**.52**	-.32	-.05	-.37	.03	-.18	-.11	-.17	-.06
Sleep 1	-.31	**.59**	-.18	-.30	.09	-.19	-.04	-.20	-.10
Sleep 2	-.30	**.70**	-.20	-.39	.07	-.25	-.16	-.33	-.13
Sleep 3	-.27	**.55**	-.11	-.28	-.04	-.15	-.07	-.18	-.12
Sleep 4	-.23	**.67**	-.17	-.39	.07	-.18	-.11	-.17	-.04
Social 1	-.11	-.17	**.17**	-.09	.03	-.10	-.01	-.04	-.07
Social 2	-.20	-.16	**.41**	-.15	.09	-.09	-.18	-.17	-.07
Social 3	-.02	-.07	**.18**	-.06	.11	-.02	-.12	-.06	.02
Social 4	-.02	-.10	**.20**	-.09	.08	-.11	-.19	-.14	-.07
Daily 1	-.55	-.35	-.16	**.61**	.09	-.34	-.03	-.25	-.24
Daily 2	-.29	-.29	-.05	**.41**	-.01	-.20	-.06	-.24	-.16
Daily 3	-.47	-.30	-.15	**.60**	.03	-.38	-.07	-.27	-.28
Daily 4	-.41	-.33	-.08	**.47**	.08	-.27	-.09	-.21	-.23
Sex 1	.00	.00	.11	.03	**.71**	.21	.10	-.02	-.08
Sex 2	.01	.11	.06	.10	**.71**	.26	.13	.03	-.09
Vitality 1	-.13	-.07	-.18	-.12	.13	**.31**	-.47	-.15	.00
Vitality 2	-.14	-.20	.01	-.29	.09	**.38**	-.08	-.21	-.15
Vitality 3	-.21	-.15	-.06	-.24	.21	**.46**	-.45	-.14	-.08
Vitality 4	-.25	-.23	-.13	-.41	.19	**.54**	-.26	-.33	-.27
Happiness 1	-.08	-.07	-.08	-.09	.07	-.37	**.68**	-.15	-.02
Happiness 2	-.10	-.08	-.14	-.04	.13	-.33	**.75**	-.17	.00
Happiness 3	-.11	-.14	-.08	-.08	.09	-.41	**.74**	-.17	-.01
Happiness 4	-.07	-.10	-.17	-.07	.04	-.34	**.67**	-.20	-.07
Depressive 1	-.17	-.19	-.05	-.17	.03	-.22	-.17	**.33**	-.18
Depressive 2	-.11	-.13	-.01	-.19	-.20	-.05	-.02	**.22**	-.25
Depressive 3	-.19	-.22	-.19	-.30	.07	-.37	-.28	**.46**	-.39
Depressive 4	-.19	-.23	-.13	-.29	.09	-.23	-.07	**.41**	-.33
Anger 1	-.16	-.14	-.11	-.29	-.12	-.23	-.09	-.43	**.39**
Anger 2	*-.10*	*-.05*	*-.04*	*-.16*	*-.08*	*-.04*	*.08*	*-.13*	***.20***
Anger 3	-.11	-.12	-.04	-.26	-.05	-.22	-.12	-.35	**.43**
Cronbach α	.74	.81	.34	.73	.83	.64	.86	.50	**.49**

Note. Number in bold indicate coefficients obtained from the corrected item-total correlation

HRQoL of Indonesian patients with DSD

Study design

This is a cross-sectional study to evaluate HRQoL of Indonesian children, adolescent, and adult patients with a DSD who had entered medical services late in life.

Participants

Patients with DSD. This group comprised 118 patients diagnosed with DSD: 60 children (42 boys, 18 girls; aged 6-11), 24 adolescents (15 boys, nine girls; aged 12-17), and 34 adults (20 men, 14 women; aged 18-41). All patients had been born with a DSD condition, were age 6 or older and the majority only recently had become under medical attention. We excluded patients born with multiple congenital anomalies, patients with non-mosaic sex chromosome DSD, and patients with DSD and intellectual disabilities (indicated from parent reports on their child's academic achievements and/or observed by the medical doctor in interaction with the patient). Of the 168 eligible patients, 21 patients (12.5%) were lost to follow-up due to relocation to other islands or invalid contact details, and 29 patients (17.3%) declined participation without specific reason. Table 5 summarized the diagnostic characteristics of the 118 patients in the study. Of 118 patients, 61 patients (51.7%) had received some treatment, whereas 57 patients (48.3%) had not received any medical treatment prior to this study. Medical treatments comprised hormonal medication and genital surgery.

Matched controls. This group comprised 118 individuals: 60 children, 24 adolescents, and 34 adults. For each patient, a healthy subject matched for age, gender, and residential settings (rural, suburban, or urban area) was found. Control subjects were identified as they were healthy, had been raised in the same gender as the matched patient, were about the same age and were living in a similar residential settings (rural, suburban, or urban area), reflecting to be raised under similar socioeconomic conditions. Three siblings joined the study, the remaining matched control subjects were approached through the local leaders (in *Bahasa: Pak RT* or *Pak Lurah*) or midwives. After a potential matched control subject was identified, information about the study followed by an invitation to join the study were given. After the control subjects gave their written consent to participate in the study, data collection was conducted following the similar procedure as the patients did.

Table 5 Clinical diagnosis of patients in the study

DSD diagnoses	Children	Adolescents	Adults	Total
46,XX CAH-SV [a]	18	2	4	24
AIS [b]	5	5	6	16
Gonadal dysgenesis [c]	12	7	16	35
46, XX Cloacal exstrophy	-	1	1	2
Androgen action disorder (AAD) [d]	13	6	3	22
Under masculinization unknown cause [e]	12	3	4	19
Total	**60**	**24**	**34**	**118**

[a] Congenital adrenal hyperplasia, simple virilizing type. CYP 21 mutation was confirmed (Juniarto et al., 2013).

[b] Androgen insensitivity syndrome. AR gene mutation was confirmed (Juniarto et al., 2013).

[c] A condition in which patients had abnormal hormonal testicular function with uni/bilaterally undescended testes. Androgen action was presumed to be fully effective. The clinical and biochemical presentation suggest gonadal dysfunction. Serum levels of luteinizing hormone and follicle stimulating hormone were elevated but testosterone, anti-müllerian hormone, and Inhibin are low for age, and no or diminished serum testosterone response to HCG.. Including in this group is patients with chromosomal DSD

[d] 46,XY DSD and disorder in androgen action. All subjects had undervirilization (EMS < 9) and normal hormonal testicular function with uni/bilaterally undescended testes. We presume, in these patients, androgen actions not to be fully effective. The clinical and biochemical presentation were close to those of subjects with a mutation in the androgen receptor with elevated serum levels of luteinizing hormone, levels of testosterone, and anti-müllerian hormone but a mutation in the androgen receptor but a mutation in the androgen receptor could not be confirmed despite extensive analysis (Juniarto et al., 2013).

[e] Under masculinization unknown cause refers to 46,XY DSD male undermasculinization (EMS > 9) with unknown cause could be identified despite extensive analyses. Serum hormone values and response to HCG were all normal for age.

Procedures

This psychological study was part of the medical study evaluating the clinical diagnoses of patients with DSD. The psychological follow-up was carried out between March 2007 to May 2011 and involved patients with DSD who were referred to the Sexual Adjustment Team from the Dr Kariadi Hospital and the Faculty of Medicine of the Diponegoro University , Semarang, Indonesia. The DSD diagnosis was based on the results of physical examination, cytogenetic analysis, hormonal analysis, and molecular analysis for gene mutations. The diagnostic procedures leading to the diagnosis of DSD have been described separately [6]. Patients were invited to participate in the study and were given oral and written study information by a medical doctor (AZJ). After patients had given written consent, an appointment was made for the psychological assessment. The assessment was conducted by a clinical psychologist (AE) in the hospital or at home. She had been trained to deliver these measures and to conduct interviews with patients with DSD. In addition to the measures applied, the history of gender development was also obtained during the interview.

Measures

See previous description about measures applied in this study. In addition to the data on HRQoL, we also collected data on socio-economic status, ethnic, and cultural background, including age, gender, residence, ethnicity, religion, education (the highest level attained), and occupation. Some of the patients changed their social gender role [13]. These patients were assessed as female or male according to the gender in which they were living in at the time of study.

Statistical Analysis

Outcome measures were compared between patients and healthy controls and between patients and healthy controls stratified for gender. Differences in continuous data with skewed distributions between two groups were summarized as median (*Mdn*) and tested with the Mann-Whitney U test. Differences in categorical data between groups were compared using Fisher's Exact test. Differences between groups were considered significant at $p<.05$ (two sided). Due to the small number of cases in subgroups, comparisons of different subgroups of DSD diagnoses, or between patients who had changed their gender and patients who did not, or between treated and untreated groups of patients were not feasible.

Results

Participant characteristics

The patients and the matched control subjects were comparable with respect to socio-demographic and cultural variables. Table 6 summarizes the background of participants in the study. The majority of participants was male, lived in rural areas, came from the Central Java province, was Javanese and Moslem. The parents' educational background varied from illiterate to university level with the majority having attended high school. Most parents worked in the low-income sector or were unemployed, particularly parents of patients with DSD.

Table 6 Socio-economic and cultural background of study participants

Characteristics background	Patients with DSD (*n*=118)	Matched Controls (*n*=118)	*p*
Age of study	13.8 ± 7.4	14.2 ± 7.1	.69
Region			
Central Java province	100 (84.7)	108 (91.5)	.12
Other provinces in Java	12 (10.2)	9 (7.6)	
Outside Java island	6 (5.1)	1 (.8)	
Ethnicity			
Javanese	108 (91.5)	106 (89.8)	.82
Non Javanese	10 (8.5)	12 (10.2)	
Religion			
Islam	112 (94.9)	108 (91.5)	.44
Non Islam	6 (5.1)	10 (8.5)	
Education – Father*	*n* = 116	*n* = 114	
Illiterate	18 (15.5)	15 (13.2)	.62
Elementary school	38 (32.8)	31 (27.2)	
High school	49 (42.2)	58 (50.9)	
University education	11 (9.5)	10 (8.8)	
Education – Mother*	*n* = 116	*n* = 117	
Illiterate	22 (19.0)	14 (12.0)	.33
Elementary school	38 (32.8)	34 (29.1)	
High school	48 (41.4)	58 (49.6)	
University education	8 (6.9)	11 (9.4)	
Occupation – Father*	*n* = 116	*n* = 114	
Unemployed	6 (5.2)	5 (4.4)	.06
Labor	64 (55.2)	46 (40.4)	
Self-employed	19 (16.4)	34 (29.8)	
Staff / Office job	27 (23.3)	29 (25.4)	
Occupation – Mother*	*n* = 116	*n* = 117	
Unemployed	57 (49.1)	39 (33.3)	.02
Labor	32 (27.6)	35 (29.9)	
Self-employed	12 (10.3)	28 (23.9)	
Staff / Office job	15 (12.9)	15 (12.8)	

Note. Data presented in *n* (%), except age: in mean ± SD. The Fisher's exact test was applied; significant at $p < .05$.
* indicates differences in *n*.

In addition to these socio-economic background, 21 patients have history of social gender role change (4 children, 2 adolescents, and 15 adults), including one child with 46,XY karyotype, raised as girl, reported gender dysphoria at the time of study, and 5 out of 34 adults with DSD are married.

HRQoL in children with DSD

Table 7 summarizes the results of comparison analysis on data obtained with TACQOL PF 6-11 year and TACQOL CF 8-11 year. Parents of children with DSD reported more problems with cognitive or school performance, social functioning, and less positive moods in their children than parents of the

matched control children did. Children reported just like their parents did; children with DSD indicated more problems in social functioning and less positive moods than the matched control children did.

Table 7 Health-related quality of life in children: Data from TACQOL PF 6-11 and TACQOL CF 8-11

Scales	Patients with DSD	Matched controls	*p*
Parent reports (PF 6-11yr)	*n* = 60	*n* = 60	
Cognitive functioning [a]	30.5 (6-32)	31 (16-32)	**.05**
Boys	31 (12-32)	31 (16-32)	.33
Girls	30 (6-32)	31.5 (24-32)	**.02**
Social functioning	27 (17-32)	30 (21-32)	**<.001**
Boys	27.5 (17-32)	29.5 (21-32)	**.001**
Girls	27 (22-32)	30 (24-32)	.08
Positive moods	12 (5-16)	14.5 (8-16)	**.008**
Boys	13 (5-16)	14 (8-16)	.23
Girls	11.5 (6-16)	15 (8-16)	**.003**
Negative moods	12 (5-16)	12 (6-16)	.71
Boys	12 (5-16)	12.5 (7-16)	.65
Girls	11 (8-16)	12 (6-16)	.98
Child reports (CF 8-11yr)	*n* = 36	*n* = 36	
Cognitive functioning	29 (18-32)	30 (18-32)	.06
Boys	30 (18-32)	30 (18-32)	.65
Girls	25 (20-32)	30 (26-32)	**.008**
Social functioning	28 (22-32)	31 (23-32)	**.03**
Boys	28 (24-32)	32 (23-32)	**.03**
Girls	30 (22-32)	30 (25-32)	.80
Positive moods	13 (7-16)	15 (8-16)	**.02**
Boys	13 (7-16)	15 (9-16)	**.03**
Girls	13 (8-16)	14 (8-16)	.50
Negative moods	15 (7-16)	13 (4-16)	.11
Boys	14 (7-16)	13 (5-16)	.66
Girls	15 (9-16)	11 (4-16)	**.047**

Note. Data presented in Median (range). Higher scores indicate higher functioning. The paired Wilcoxon signed-rank test was applied; significant at $p < .05$ [a] $n = 56$ subjects; four children did not enter the school yet.

More detailed analyses on differences between boys and girls revealed that problems in social functioning were particularly reported by parents of boys and by the boys themselves. Boys with DSD also reported less positive moods. Parents of girls and girls themselves indicated problems in cognitive or school performance. Parents reported less positive moods in their daughters but the daughters reported less negative moods.

HRQoL in adolescents with DSD

Table 8 shows the results of comparison analysis on data obtained using the TACQOL PF 12-15 and TACQOL CF 12-15. The results show that parents of adolescents with DSD and parents of matched control groups reported

equally with respect to the HRQoL of their children. Adolescents themselves reported accordingly. Adolescents with DSD did not significantly differ from the matched control adolescents in reporting problems related to cognitive and social functioning as well as positive and negative moods.

Table 8 Health-related quality of life in adolescents: Data from TACQOL – 12 -15

Scales	Patients with DSD	Matched controls	*p*
Parent reports (PF 12-15yr)	*n* = 19	*n* = 19	
Cognitive functioning	32 (25-32)	32 (28-32)	.34
Social functioning	30 (24-32)	30 (16-32)	.59
Positive moods	13 (8-16)	14 (6-16)	.99
Negative moods	14 (8-16)	14 (8-16)	.41
Adolescent reports (CF 12-15yr)	*n* = 19	*n* = 19	
Cognitive functioning	31 (24-32)	32 (20-32)	.90
Social functioning	32 (24-32)	32 (14-32)	.95
Positive moods	14 (7-16)	14 (4-16)	.97
Negative moods	15 (8-16)	13 (3-16)	.18

Note. Data presented in Median (range). Higher scores indicate higher functioning.
The paired Wilcoxon signed-rank test was applied; significant at $p < .05$

HRQoL in adults with DSD

Table 9 presents the results of the comparison analysis on data obtained using the TAAQOL. Adults with DSD reported more depressive moods and less angry moods than the matched control adults. Women with DSD reported less angry moods, whereas men inclined to report more depressive moods, compared to their matched control adults.

Table 9 Health-related quality of life in adults: Data from TAAQOL (16 yr or older)

Scales	Patients with DSD	Matched controls	*p*
	n = 39	*n* = 39	
Cognitive functioning	81.2 (0-100)	81.2 (6.2-100)	.79
Sleep problems	81.2 (0-93.7)	81.2 (0-93.7)	.84
Social functioning	93.7 (0-100)	93.7 (50-100)	.51
Daily activities	100 (12.5-100)	100 (37.5-100)	.94
Sexuality [a]	87.5 (12.5-100)	100 (50-100)	.45
Feelings of vitality	50 (0-100)	50 (8.3-100)	.58
Positive moods	66.7 (8.3-100)	66.7 (16.7-100)	.73
Depressive moods	66.7 (0-100)	83.3 (25-100)	**.05**
Men	65.9 (25-100)	83.3 (25-100)	.06
Women	66.7 (0-100)	70.8 (25-100)	.36
Angry moods / aggressive emotion	88.9 (11.1-100)	77.8 (33.3-100)	**.02**
Men	88.9 (11.1-100)	77.8 (33.3-100)	.50
Women	94.4 (55.6-100)	55.6 (33.3-100)	**.003**

Note. Data presented in Median (range). Higher scores indicate higher functioning. The paired Wilcoxon signed-rank test was applied; significant at $p < .05$

Discussion

This study aimed to investigate the HRQoL of Indonesian patients with DSD in whom DSD had been identified late in life. As a consequence, these patients received limited or no treatments and education about their DSD condition and its consequences. In most cases, patients with DSD did not report physical impairment or disabilities. However, they may experience social stigmatization due to ambiguities of genital, body, or gender. The majority of studies on QoL in Western patients with DSD have been conducted in patients who had received medical treatment early in life. To date, no study about QoL in late identified or untreated patients with DSD had been conducted in Indonesia. By assessing HRQoL of patients with DSD, we could gain insight on the patients' health status and the emotional impact of DSD in their lives. Our findings indicate that DSD impaired social and emotional functioning of patients, particularly children and adults.

In children with DSD, different types of problems were identified. Parents observed that children with DSD raised as boys showed more problems with social relationships (i.e. peers, parents) than matched control boys. However, in children with DSD raised as girls, parents observed that their daughters were less happy and showed more problems with cognitive functioning than parents of matched control girls observed their daughters. This finding can be explained as the majority (15 out of 18) of young girls in this study have 46,XX CAH. Moreover, this group also included one girl with 46,XY karyotype who reported dissatisfaction with the assigned gender. We observed that gender identity confusion was evident among these children with DSD raised as girls, but not in young patients raised as boys [13]. This can be understood because in girls with 46,XX CAH, prenatal exposure of androgens masculinize body, including genitalia, and influence male gender role behavior in later life[14]. Being born with an ambiguous genitalia, growing up with muscular bodies, and displaying preference on masculine type of toys/interests may cause these young girls with 46,XX CAH to be confused which may subsequently influence their gender identification [13].

In Indonesia, DSD is not known in the general population. Although the old term of hermaphrodite is known, in local language it is misperceived as "double genitals" (in *Bahasa: kelamin ganda)*. In our previous study we reported that patients with DSD in Indonesia were often mistakenly perceived

as transgender persons; therefore they often became subject of social stigmatization i.e. being teased by their peers, classmates, or neighbors[15]. In previous studies, we observed that children as well as older patients with DSD who had a visible DSD features experienced social stigmatization from peers or neighbors which were stressful for them[15]. Furthermore, children with DSD raised as boys displayed more externalizing problems, aggressive behavior, and social problems, as shown by the Child Behavior Check List (CBCL) scores; whereas adults with DSD reported anxiety and feeling depressed as shown by the Adult Self-Report (ASR) scores[16].

Adults with DSD reported more depressive moods and less angry moods than matched control adults did. This finding is in line with findings from our previous study [16]. Further investigation revealed that adults with DSD were sexually distressed, very dissatisfied with their sex-related body parts, and worried about their future, particularly in relation to marriage and infertility. Fear of rejection from potential partners made them limit their social relationships[17]. Being raised in a collective society, Indonesian patients with DSD as well as other society members, are exposed to strong demand to follow social norms and expectancies from early life onward[18, 19]. Failure to meet social demand is considered shameful for individuals as well as the family[20]. As the majority of patients come from a poor family, have limited educational background, and lack of knowledge about DSD, it is difficult for them to make sense regarding the ambiguities in their bodies, genitals, or gender role behavior, all caused by DSD. Consequently, they failed to explain their condition to other people in their community, who also have a lack of knowledge about DSD. This, leads to social rejection as well as to social withdrawal of the patients [13, 15, 17]. Therefore, we conclude that DSD impact greatly on social and emotional functioning of Indonesian patients with DSD, particularly children and adults. Moreover, findings in the study also indicate that cognitive functioning of children with DSD raised as girls are impaired. Unfortunately, in this study, we could not compare the cognitive functioning scores of patients with 46,XX CAH raised as girls with patients of different DSD diagnoses (i.e. 46,XY DSD raised as girls, or 46, XX raised as boys), due to small sample.

In this study, no significant differences were found among adolescents with DSD and the matched control adolescents. This is aligned with the findings from study on emotional and behavioral problems among adolescent patients with DSD where we also found no significant differences with the matched

controls [16]. We assume that adolescents may have ignored or refused to acknowledge problems, as they want to be regarded as adults. On the other hand, parents may be more tolerant to problem behavior in adolescence. Therefore, problems may be underrated by adolescents and their parents as well. Study on adolescents German with DSD reported that in general, the psychological well-being of these adolescents were not impaired, except concerning sexual relationships[3]. Unfortunately, studies on adolescents patients with DSD is lacking, therefore we could not explain our findings. Further studies should investigate more thoroughly additional factors related to psychological well-being of adolescent patients with DSD, e.g. sexual debut.

Findings in this study need to be interpreted by considering the following limitations. *First,* the TACQOL/TAAQOL have been widely used on patients with different diseases and have been compared to a large reference population. We could not do similar comparison in this study, but at this stage, we able to assess the validity and reliability of the Indonesian version of the TACQOL/TAAQOL and therefore we obtained a general overview on the HRQoL of patients with DSD. *Second,* as no single measure could be used and in view of lack of uniformity in clinical management (types of DSD diagnoses, types of treatment, differences in gender of rearing), it was not possible to conduct detailed comparison analyses i.e. comparing patients with different DSD diagnoses raised as males or females. *Third,* despite the scale adaptation procedure that we applied, the validity and reliability of the Indonesian version of TACQOL CF 8-11 is less satisfactory compared to the original version. We assumed that young children in our study (aged 8-11) may be too young to evaluate themselves using the non-dichotomous response mode; but such experience was not reported before. Interestingly, our data on TACQOL CF 8-11 are in line with data on parent-report, and altogether, findings from TACQOL PF/CF 8-11 are in line with findings from previous studies reporting emotional and social problems[13, 15, 16]. Therefore we decided to report our data on TACQOL CF 8-11 and interpret carefully. By doing so, we hope that our experience would be a useful lesson-learned for Indonesian researchers, or international counterparts, who are willing to pioneered a psychological research in a rare-disease, like DSD, in Indonesia. Fourth, as no DSD-specific measures on health-related quality of life is available, findings from our study using a generic measures may overlook problems affected by DSD. Future studies are expected to developed a diagnoses-specific measure of HRQoL for patients with DSD.

In conclusion, this study reported HRQoL of children, adolescents, and adults with DSD. The majority of patients did not received medical attention in early life and had to cope in social life with an ambiguous body and/or gender with limited understanding about their DSD condition [15]. This study revealed that young patients experience more barriers in their social contacts and felt less frequently happy, whereas depressive moods is prominent in adults. Children with DSD raised girls showed problem with cognitive functioning; the majority of these young girls have 46,XX CAH. Interestingly, findings from this study are complement to findings reported from previous studies that demonstrated emotional and social problems. Therefore, we conclude that the HRQoL of children and adults with DSD is impaired, but not in adolescents. DSD impacts social and emotional functioning of children and adults. We assume that a better HRQoL may be achieved by early establishment of a definitive diagnosis and moreover by education and medical treatment to prevent body ambiguity. These findings support the importance of referral of persons with DSD to a specialized center for treatment in early life. Psychological assessment and counseling should be integrated in the patient's treatment plan as well as long term follow-up into adulthood.

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RUMAH ADAT
BAANJUANG

Chapter 8

General discussion

General discussion

The management practice of patients with a DSD in Western countries differs greatly from those approaches applied in Asian countries[1]. Late presentation, delayed identification, lack of diagnostic facilities and treatment options, and lack of expertise have been reported as a major challenges in management of DSD in poor-resource countries[1-4]. It was argued that poverty and cultural aspects influence the management practices between Western and non-Western countries differently [1]. Poverty makes health-care facilities not only being less available but –if available- also less accessible for poor patients. Cultural background and social context influence patients' as well as health-care professionals' cognition about illness and their decision in dealing with it. In poor-resource countries of Asia, it is common that children born with ambiguous genitals grow up with their original anatomy due to unaffordable medical treatment or cultural acceptance [1,4]. As many people with disabilities in these societies remain untreated, people are accustomed to regard this as the only option feasible for them. They may seek medical advice when a problem escalates, which in the case of DSD is often in adolescence or adulthood. How do children, adolescents, and adults with DSD deal with such situation? Are they treated with respect and dignity that would allow them to grow-up with self-confidence? Are they empowered to make their own decisions on treatment, surgery, and even gender identity?

The aim of our study was to investigate gender development, emotional and behavioral functioning, social stigmatization, body image, sexual functioning and sexual orientation, as well as health-related quality of life in patients with DSD in Semarang, Indonesia who, for a long time, had been lived with limited or no medical care. DSD is not widely known; neither by medical professionals nor the general population of Indonesia. Therefore genital anomalies or other signs of DSD are not recognized; and if they are recognized, referral to a specialized medical center stays out, either because the medical professionals are unaware or the patients are uninformed to refer themselves. Consequently, they have been living in an ambiguous body and gender, without sufficient or proper information and treatment for their DSD condition. In Western countries, most of the patients with DSD were identified and treated early in life. Nevertheless, previous studies performed in Western countries have reported psychological problems despite of medical

treatment provided in early life[5-7]. As in this decade, only few Western patients with DSD are untreated or treated lately, which limits studying the course of psychosexual development and psychological well-being in these patients. In fact, the course of DSD and its associated psychological consequences by types of DSD is essentially unknown. In working within a multidisciplinary team treating patients with DSD in Semarang-Indonesia, we were confronted by many parents and patients with questions regarding gender assignment and reassignment, gender of rearing practices, infertility, and sexuality functioning. They had problems in having romantic relationships and wanted answers for emotional and behavioral problems of their children. Patients suffered from social stigmatization and had problems in accepting their DSD condition. Their questions and concerns formed the basis of this psychological study. In fact, this is the first psychological study reported among Indonesian patients with DSD.

Study limitation

Development of local instruments

Our intention was to compare the findings from our study with findings from available studies, mostly performed in patients with DSD in Western countries. Prior to the study onset, no relevant measures were available in the local language. Therefore, we searched for measures that were used in comparable studies reported from Western countries which have proven satisfactory psychometric properties, and translated the measures into local language (*Bahasa Indonesia)*. For this purpose, we followed procedures for semantic and cultural adaptation of the internationally available measures and assessed the psychometric properties of the Indonesian version of measures used in the study using healthy normative groups. We also performed pilot testing prior to implementation. Unfamiliarity with self-report measures and illiteracy were barriers that we encountered as the majority of our patients are poor, came from rural area, and have limited education. We learned that it was best to apply measures orally, as a structured interview. In general, the psychometric properties of the Indonesian measures used in the study were satisfactory. Few questions that was not applicable or need improvement in the future were identified and reported.

Cross-sectional study of patients and matched controls

Our study was designed a study of patients with matched controls. We encountered serious difficulties to fulfill the matching criteria for the healthy matched control subjects. Initially we planned to enroll siblings as the matched control, however, this most often were unfeasible due to differences in gender, no sibling, or disapproval to involve sibling in the study. Subsequently, matched control subjects were piled up from healthy control subjects lived in the similar neighborhood with the patients, which were contacted through the local leaders and then invited to join the study. These practices might be uncommon or differs greatly from common practice applied in psychological research in Western countries.

Heterogeneity of DSD, patients and clinical management

The third pitfall is related to lack of uniformity in clinical management of patients with DSD in our study. Although 118 subjects seemed sufficient for comparison, different types of treatment, DSD diagnoses and clinical features, as well as differences in gender (including changes in gender role) across age group (children, adolescents, and adults), prevented us from conducting stratified analysis with a sufficient number of subjects and statistical power. It is therefore impossible to state if emotional problems, gender identity, stigmatization and quality of life differ by subgroup of patients, type of DSD and treatment status. However, our findings are highly valuable at least in descriptive terms, as the reported outcomes were obtained mostly from untreated patients, whom are rarely seen in this decade.

Major findings in Indonesian context

The birth of a baby with ambiguous genitalia can be stressful for parents because often gender assignment is delayed and parents have to cope with an awkward moment when they cannot answer to the most common question "Is your baby a boy or a girl?". In our study on social stigmatization, we found that patients born with ambiguous genitalia, particularly those who are living in a small village, most often could not avoid being identified with DSD [11]. As ambiguous genitalia is very rare and DSD is not known widely, the birth of a newborn with an ambiguous genitalia shocked neighbors and family members, spread out throughout the village, and soon, both baby and the affected family become object of social attention, even until the baby has grown up [11]. In

young children, particularly girls with 46,XX CAH, gender identity confusion and masculine gender role behavior were reported [8]. In some patients, their DSD was unknown to others, except their parents. Children may not fully be aware of the social expectations or pressures surrounding them, but at some moment, children with DSD found out that they are different from others (e.g. boys with hypospadias could not urinate by standing or could not have circumcision as other boys of similar age had; girls with CAH present themselves as tomboy girls despite parents' efforts to dress them as feminine girls). As we observed in our study on stigmatization, the adults people rarely stigmatized children with DSD, but they addressed their positive (supporting) and negative (stigmatizing) behavior to the parents, i.e. they blamed the parents for delayed help-seeking, insulted parents for having a boy with an imperfect penis, supported parents by giving information or raising funds for medical treatment. However, children who have their DSD condition known by others were often being teased by their peers as they were mistakenly perceived as transgender children. They called them *"banci" (Bahasa:* male transvestite), made them a joke, and refused to play with them. Neither the child or the parents know how to deal with this problematic situation [11]. Lack of knowledge about DSD makes patients and parents confused with the child condition and thus it is difficult for them to explain the DSD condition to others. As children spend most of their daily time, at school as well as at home, to play with peers, it is not surprising that young patients in this study reported to be less happy, conducted more aggressive behavior, and reported more problems in their social relationships (i.e. peers, parents) compared to matched control children [10,12].

It should be mentioned that not all adolescents with DSD received social stigmatization. Patients in whom their DSD features were not visible or can be hidden (i.e. under their clothes) most often reported less stressful than patients with visible DSD features because no one was aware of their DSD [11]. Therefore, this group of adolescents keeps hanging out with their peers and involved in social activities like their peers. However, during this period puberty takes place. Bodily changes, sexual attraction, and peer pressure begin to play a role in adolescent's life. Adolescent patients, whose DSD was known since childhood, were still being teased (called *'bencong' –banci* in Javanese language*)* [11]. In our study on gender development [9], we observed that patients who later changed their social gender role in the adulthood, developed gender dysphoria during adolescence, but they did not share their confusion to their parents until

adulthood. Two out of 24 adolescents with DSD changed their social gender role at the aged of 17. In these patients, emotional problem were evident [9]. These may explain the lack of significant differences we observed between adolescents patients and matched control adolescents in view of emotional or behavioral problem and health-related quality of life [10,12]. Adolescents experience great changes, bodily as well as emotionally and socially in their transition to adulthood. They are more aware of peer conformity but not yet fully aware of social expectation in their future life as adult.

Being unidentified of having a DSD does not imply that emotional problems are less or absent. Adult patients as well as parents of youngsters with DSD told their worries about future, mainly about marriage, infertility and reproduction, and limited finance to afford medical treatments or surgeries [11]. In Indonesian society, marriage is a precondition for becoming a fully respected member of society and parents have great responsibility to initiate their children's marriage [13]. The newly-wed couples are expected to have children soon after being married. It is common that friends, relatives, or neighbors ask them for signs of pregnancy to show their caring, whereas in Western society this practice would be considered as rude or disrespectful to one's privacy. Our study also revealed that social consequences are far more severe for infertile women than for infertile men. We assumed that it is easier for men than for women to hide their infertility from society [8]. Being unmarried, particularly for a woman, is considered bringing shame to the family [14]. Shame is a vital element in Javanese culture[14]. In adulthood, social expectations will be intensified. As Javanese people have been taught to follow social norms [13], patients who had delayed seeking medical help or who were not aware of their DSD, began to take action to solve their problem. About the onset of adolescence, they began to inform their parents about their genital or body ambiguities, seek job to fund their treatment, or visit the medical doctor for examination. In some adults with 46,XY karyotypes assigned female at birth, their body ambiguity and sexual attraction to persons of the opposite gender confused them [8,9]. Most of them have no other option deal with than confronted with the unpleasant response given by their classmate, neighbors, or relatives through verbal and behavioral stigmatization [11]. Having insufficient understanding about the changes occurring in their body and mind, these patients decided to give it a try to live in the opposite gender by moving to other regions and start living in a new identity. Testing themselves by having a real-life experience in living

in the opposite gender seemed to have helped these patients to reduce their tension and confusion in dealing with the ambiguous body and gender. From our study on adult patients who underwent a social gender role change in the past 2-25 years, we observed that they reported severe gender-related problem during period of their living as female, but they are satisfied with their gender identity and gender role behavior during their living as men [9]. We assumed that their satisfaction with male gender identity and gender-role behavior might have been influenced by the reduced stigmatization and/or the increased acceptance of the community. More men than women with DSD are married or have romantic relationships and received acceptance and emotional support from their partners and their families, whereas women with DSD tended to avoid romantic relationships, and experienced more sexual distress. One woman even received a divorced plea due to her infertility. Despite these differences, both men and women with DSD reported dissatisfaction with their sex-related body parts, have fear of rejection from potential partners, and are concerned with their infertility [8]. Being aware of the possible failure to meet social expectations in the future, might explain that emotional problems, as in anxiety, depression, and internalizing problem are more frequently seen in adult patients with DSD than matched control adults, as we observed in our study on emotional or behavioral problem and health-related quality of life [10,12].

Conclusions

Based on the findings derived from our studies, we conclude that a DSD condition has great impact on many psychological aspects of our patients across gender and developmental stage. Our studies demonstrate that patients with DSD who had received limited or no treatment for their DSD condition experienced gender-related problems, sexuality-related problems as well as, emotional and behavioral problems. Health-related quality of life was also impaired, particularly in children and adults with DSD. They were unhappy depressed and showed problems with social relations. Moreover, patients with visible DSD characteristics experienced social stigmatization and reported stress due to this stigmatizing experience. A large number of patients with DSD underwent female-to-male social gender role change, mostly as adults but also occurring during adolescence and childhood. Many of these patients

experienced major problems related to their gender identity development. The change of gender was felt as a great relief and reduced the gender problems. Such large percentages of patients with a wish for a social gender role change are not observed in countries and areas that offer diagnostic evaluation and treatment just after identification of an ambiguous genital or ambiguous body development.

Having a DSD condition, being infertile and fear of being rejected caused significant distress, particularly among women. Late-treated patients experienced similar problems as untreated patients. Ambiguity of genitals, body, gender, and appearance elicited stigmatization in patients with DSD. Having a visible DSD characteristic, living as a female, and living in rural areas in Indonesia made that person vulnerable for social stigmatization. Children and adults with DSD reported emotional and behavioral problems: internalizing problems were evident, particularly among untreated patients, and were not associated with specific DSD diagnoses. Early referral to a multidisciplinary team is crucial for patients to receive appropriate treatment soon after the identification of DSD. Education on DSD and its consequences is pivotal for patients as well as for laymen. For patients with DSD and their families (parents), education about DSD should also directed to improve their social skill in dealing with social problems encountered in daily lives.

As patients with DSD interact with their society, there is impact from society on patients' problem and experience. In a collective-driven society like Indonesia society exerts more power than individuals in the sense that they contribute to people's cognitions, attitudes, and behaviors [15]. Javanese, the major ethnic in Indonesia, emphasizes on social bonds, particularly in a village [13]. People know each other very well and share their concern about anything. "What people will say or do?" does matters, and DSD is no exception in that regard as the findings from our study show. Therefore it can be understood that problems with social functioning and emotions were evident among Indonesian patients with DSD across our studies. Children reported difficulties in dealing with peers or parents as is shown from the TACQOL and CBCL scores; whereas adults, particularly women, often withdrew themselves from social contacts and even refused to enter romantic relationships. Depressive mood, sadness, and unhappiness were also prominent among our patients with DSD. Living with a DSD is hard and even harder for patients who live in society which does not understand nor supports patients with a DSD.

Being a member of society is part of personal identity, and so does gender. Being neither male nor female is uncommon in Indonesian society, unless the person is known as *'waria, banci, wadam'* (Indonesian term for male transvestite) or '*bencong or wandu*' (Javanese terms for male transvestite)[16]. None of these term are respectful. Being labeled with these terms imply strong message of social exclusion, which is painful, as reported by patients who experienced different forms of social stigmatization due to their DSD condition. It is obvious that there is a lack of proper knowledge about DSD in the society. As a consequence, patients with DSD features that are visible to other people (i.e. girl with a virilized body, ambiguous genitalia in newborn) experienced social stigmatization in a way that was stressful for them, or patients with concealable DSD features anticipated such stigmatization by delayed help-seeking. However, as we learned from our study on stigmatization, there are few patients that received social support and acceptance when they received reliable information about DSD from the medical doctors. It indicates the possibility of promoting social acceptance for patients with DSD by giving a proper and reliable information about what DSD is and what it is not.

Recommendations

We recommend to provide education about DSD to three targeted groups. *First,* to health care providers involved in first line medical care to facilitate referral of patients with suspected DSD for medical treatment. *Second,* giving information about DSD and its consequences to patients and parents, or their family members, to facilitate acceptance of DSD in the family. *Third,* providing reliable information about DSD to Indonesian society.

In primary care centers in Indonesia (*'Puskesmas* or *Posyandu'*), general practitioners, midwives, and nurses play important roles in educating patients or people in their particular neighborhood. Ideally, referral should be to a type A hospital which has a multidisciplinary team providing medical care for patients with DSD. The information given should cover appropriate information about DSD, its clinical and psychological impacts and instruction on how to cope with practical social consequences. The information need to be communicated in a language that is easily understood. In the past decades, the knowledge obtained from scientific research on DSD had developed rapidly. To facilitate

early referral of persons with DSD, knowledge about DSD should be integrated in the education curriculum of the medical doctor, nurse, and psychologist. The newly graduated need to be updated with the latest advancement in science and research on DSD. Considering the geographical condition of Indonesia, it will be very helpful to participate in an online learning platform offered by the European Society for Pediatric Endocrinology (www.espe-elarning.org) that provides reliable information and update research on DSD that can be accessed freely by medical doctors and other health practitioners to support their understanding on DSD. With this online learning, a collaboration between medical centers in Indonesian can be facilitated.

For patients and their family members, particularly who come from rural area with limited educational background, giving oral information with sufficient opportunities for them to address their questions and confusion to the members of multidisciplinary team is essential. This group may also receive information about DSD from general practitioners or other health-care professionals (group one) or general society (e.g. journalists, NGO activists, teachers). At present, there is no one reliable source of information on DSD that can be accessed by publicly in Indonesian language. The availability of reliable information about DSD in Indonesian language, in an online format, can be helpful to educate the general population of Indonesia in order to promote acceptance for persons with DSD.

The results of our studies highlight the importance of psychological aspects in the management of patients with DSD. The involvement of a psychologist, as well as other medical specialties, is an essential part of the multidisciplinary approach of patients with DSD. Therefore, education about DSD and its psychological impacts on the lives of patients and the affected families is essential. There is a definite need for psychological counseling and follow-up evaluation of patients. It is important for psychologists to understand that DSD is a life-long condition that requires life-ling psychological care. Long-term psychological assessment and intervention are crucial and family counseling is often needed. In the context of Indonesian culture, working with the extended family or community leaders in giving proper information about DSD might be necessary in order to facilitate patient's adjustment in the society.

Thus results of our studies strongly suggest that follow-up evaluations should be performed not only of the patients presently in their childhood or adolescence but also of adult patients. This follow up should be integrated in a

long term treatment plan which needs to be well-communicated to all involved in order to understand the importance of long term support.

At the beginning of this study, we received critics that conducting such study in a non-Western country, using Western-based measures, is impossible and unfeasible. Indeed, our study encountered challenges and barriers, like most pioneer studies do. Nevertheless, we have put considerable effort to solve the problems and remove the barriers, and made this study happen. We acknowledge limitations in our study as well as recognize opportunities for improvement in future studies[8-12]. We believe that our experiences could be a useful lesson-learned for Indonesian researchers as well as international counterparts that willing to conduct a pioneer study in psychological field, particularly focusing in a rare-disease like DSD.

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Chapter 9

Summary

Samenvatting

Rangkuman

Summary

Disorders of sex development (DSD) are not widely known among general population in Indonesia, even among health practitioners. Therefore, management of patients with DSD in Indonesian, is being challenged by lack of diagnostic facilities and expertise, availability of medical and uro-surgical treatment. There also is a lack of awareness with respect to the consequences of having a DSD condition and impact of late treatment. In 1989, a multidisciplinary team was setup jointly by the Dr. Kariadi Hospital and the Faculty of Medicine, Diponegoro University Semarang, in Central Java (Indonesia) to provide care for patients with DSD. The team had been confronted with questions raised by patients and parents about gender issues such as gender assignment, confusion about one's gender identity and gender dysphoria, issues on body ambiguity and sexuality , emotional problems and psychological well-being. As the majority of research on DSD reported from Western countries were conducted on early treated patients, we often could not provide relevant information to our patients. The focus of our study was: "Do Indonesian patients with DSD suffer from similar psychological problems as Western patients do and what is the impact of DSD on psychosexual development and psychological well-being in patients who only received little medical attention? This psychological study, that was conducted in 2007-2013, is part of a clinical study on diagnostic evaluation on 286 patients with DSD in Indonesia.

Chapter 1, provides an introduction to DSD particularly on the DSD diagnoses found in our study, followed by an overview on common practice of management of patients with DSD in Western and non-Western countries, including our center in Semarang. This chapter also outlines psychological aspects of DSD particularly within the context of DSD diagnoses relevant to this study.

Chapter 2 comprises information about the methods applied in of this study. As many methodological issues are also described in chapters 3 – 7, this chapter focuses mainly on methodological aspects that had not been explained in these chapters, including scale validation and construction and methodological challenges in conducting a case-control psychological study in Indonesia.

In chapter 3, we report findings on sexuality among 34 adult patients with DSD. With respect to sexuality, male and female sexual functioning, body image, female sexual distress, and sexual orientation were investigated. Our data revealed that adults with DSD were dissatisfied with the sex-related body parts such as genitals, breasts, facial hair but not with body parts that are not related to gender such as eyes, hair etc. With respect to sexual functioning, the majority of women with DSD felt sexually distressed. The women withdraw themselves from romantic relationships and refused or delayed entering a partner relationship. Compared to the women, more men had experiences in romantic and partner relationships; they were more willing to seek partners and sexual relationships, and more men than women were married. The majority of adults in the study chose a partner or was sexually attracted to a partner in opposite of the gender they have been raised in. A few partners reported sexual attraction to persons of the same gender. Our findings also showed adult patients, either men or women, were concerned with infertility. Disclosure dilemmas, marriage or having a partner, and fear of rejection were more prominent in women than men. We concluded that DSD had major impact on sexuality. It impacted differently in the lives of men and women, in accordance to different social expectations for men and women.

In chapter 4, we report on a unique study on gender development in children, adolescents, and adult patients with DSD. We investigated gender identity and gender role behavior in 118 Indonesian patients (76 males, 41 females) with different DSD diagnoses and compared findings with 118 healthy controls matched for gender, age, and residential setting (rural, suburban, or urban). In the first part we report on methodological aspects of the measures such as translation, scale adaptation and assessment of psychometric properties of the translated measures. In the second part, we report on gender outcome in 60 children (42 boys, 18 girls), 24 adolescents (15 boys, 9 girls), and 34 adults (19 men, 15 women) with DSD. The majority of patients only had received little medical attention in the past and never had received any medical treatment prior to this study. We observed a remarkably high percentage of change of social gender role: 6.7% among children; 8.3% among adolescents; 44.1% among adults. All except one patient had changed gender from female to male. Of them, 81% had a 46,XY karyotype and suffered from undermasculinization, the remaining patients had 46 XX CAH-SV. Their bodies had undergone significant

masculinization during life. Confusion about gender identity and cross-gender behavior were more frequently observed in children with DSD raised as girls than in children raised as boys and in groups. Adolescents and adults with DSD raised as females experienced more gender-related problems. An integrated clinical and psychological follow-up on gender outcome is necessary during pre-puberty and adulthood.

In chapter 5, we present our findings from a study on emotional and behavioral problems in our patient group. By means of questionnaires patients from age 11 onwards evaluated their behavior. Parents filled out questionnaires too, for youngsters aged 6 – 18. Our findings demonstrated that patients with DSD more often withdraw themselves form social contacts reported more problems related to sadness and depression than the control group did. Men reported more anxiety and depression whereas women were more withdrawn. Parents reported similar problems in their young children but in adolescence no emotional or behavioral problems were noticed, neither by adolescents themselves nor by their parents.

In chapter 6, we report on patients' experiences with social stigmatization. For more than two decades, policy on medical treatments are under debate; particularly surgical treatments performed to correct or prevent genital and body ambiguity. Such treatments have been developed to prevent social stigmatization evoked by the odd appearance Interestingly, no scientific study has been published that investigated stigmatization in DSD patients. In fact, there is no literature that support this medical practice. In this study, we applied both quantitative and qualitative methods to obtain an overview of our patients experiences with social stigmatization. We developed rating scales that measure social stigmatization. Our findings indicated that patients with visible characteristics of DSD experienced more social stigmatization than patients in whom characteristics of DSD were not visible DSD condition or could be hidden under clothes. The more patients experienced stigmatization, the higher stress such experiences evoked., Patients with visible DSD characteristics, have to deal with these social reactions. Patients in with hidden characteristics of DSD anticipated or prevented themselves from being identified by other people.

In chapter 7, we tried to find out to what extent DSD impaired the patients' quality of life. Our data in children showed that DSD, affected their social functioning; patients had more difficulties to align to other children). Their parents also indicated their children were less happy .Adult patients reported depressive moods. In contrast, adolescents and their parents did not report signs of social stigmatization. So the data on HRQoL are in concordance with findings on emotional and behavioral problems and with findings on sexual distress.

In chapter 8, all findings in the described investigations will be discussed in a broader context. Recommendation are made for an integrated approach for medical and psychological problems. Not only the somatic problems need to be attacked, patients with DSD also have to deal with or fight with many psychosocial problems. Patients can benefit from the psychologist's knowledge en experiences on coping with disease and coping sensitive issues such as being watched and isolation. As these psychosocial problems are closely related to the medical aspects of DSD, treatment will be best when the medical doctor and the psychologist collaborate.

Samenvatting

Over stoornissen in de geslachtsontwikkeling (Engels: *disorders of sex disorders*, afgekort tot DSD) is in Indonesië maar weinig bekend. Niet alleen weet de Indonesische bevolking er weinig van, ook onder artsen en verpleegkundigen is er relatief weinig bekend. Diagnostiek en behandeling van DSD zijn daardoor beperkt. In 1989, werd een multidisciplinair team is opgericht in het Dr. Kariadi Ziekenhuis en de Faculteit der Geneeskunde van de Diponegoro Universiteit in Semarang, Indonesië. Het team stelde zich tot doel de zorg voor patiënten met DSD te bevorderen. In de eerste jaren van het bestaan werd het team geconfronteerd met een veelheid aan vragen van patiënten en hun ouders over gender toewijzing en verandering van gender, gedrag dat als problematisch werd ervaren omdat het niet zou passen bij de toegewezen gender, vragen over seksualiteit, emotionele problemen en het maatschappelijk stigma waarmee patiënten en ouders werden geconfronteerd. Aangezien het meeste onderzoek naar psychosociale problematiek verbonden aan DSD is uitgevoerd in westerse landen, was het vaak onmogelijk om relevante informatie te verstrekken.
Dit onderzoek richtte zich op de vraag op de psychologische problematiek zoals die bij westerse patiënten wordt gezien, ook voorkomt bij Indonesische patiënten. De meeste patiënten die zich bij het Dr. Kariadi Ziekenhuis hadden aangemeld voor hulp, hadden weinig tot geen medische behandelingen ondergaan. Een groot verschil met westerse patiënten die, zodra een afwijking in de geslachtsontwikkeling wordt vermoed, worden verwezen voor diagnostiek en behandeling. Dit onderzoek bood de mogelijkheid om uitblijven van medisch ingrijpen op de psychoseksuele en psychosociale ontwikkeling te onderzoeken. Die vraag is ook voor westerse patiënten relevant, omdat er kritiek is op het huidige behandelbeleid. Die kritiek betreft vooral het medisch ingrijpen op jonge leeftijd, waarbij kinderen zelf nog te jong zijn om hun stem te laten horen bij de beslissingen die over hen worden genomen. Deze studie werd uitgevoerd tussen 2007 en 2013, en was onderdeel van een klinisch studie over de diagnostische evaluatie van 286 Indonesische patiënten met DSD (onderzoeker: A. Zulfa Juniarto).

Hoofdstuk 1 bevat een introductie over psychologische problematiek welke voorkomt bij patiënten met DSD, waarbij wij ons hebben gericht op de diagnoses van de patiënten die aan deze studie hebben meegedaan. Het hoofdstuk bevat

tevens een overzicht op de klinische praktijk in westerse landen, niet-westerse landen en die van het Dr. Kariadi Ziekenhuis.

Hoofdstuk 2 bevat aanvullende informatie over de opzet van de studie en de research methoden die zijn toegepast. Veel van de methodologische opzet van de studie wordt beschreven in de hoofdstukken 3 t/m 7. Omdat niet alle methodologische aspecten in de artikelen konden worden opgenomen, is er voor gekozen hier een apart hoofdstuk aan te wijden in het proefschrift.

In **hoofdstuk 3** rapporteren we de bevindingen uit het onderzoek naar lichaamsbeleving en psychoseksueel functioneren. We onderzochten 34 volwassen patiënten met DSD en vergeleken hun gegevens met die van een controle groep van 34 gezonde mannen en vrouwen die met hen gematcht waren op leeftijd, geslacht en woonomgeving. Het onderzoek liet zien dat patiënten met DSD ontevreden waren over de primaire en secundaire geslachtskenmerken, zoals het genitaal, de borsten en gezichtsbeharing. Met lichaamsdelen die niet geassocieerd zijn met sekse, zoals hoofdhaar en ogen, waren patiënten in het algemeen tevreden. Op een vragenlijst over seksueel functioneren zagen we dat vrouwen bijna geen seksuele ervaringen hadden. Ook mannen hadden weinig ervaring, maar waren actiever in het aangaan van romantische en seksuele relaties dan vrouwen. Vrouwen durfden geen relaties aan te gaan uit angst dat hun aandoening bekend zou worden. Zij vreesden negatieve reacties als bekend zou worden dat zij onvruchtbaar waren. Hun terughoudendheid in de liefde leverde veel stress op, omdat van hen werd verwacht dat zij zouden trouwen en kinderen krijgen. Ook mannen maakten zich zorgen over hun onvruchtbaarheid, maar waren aanzienlijk minder bang voor negatieve reacties. We concludeerden dat DSD het aangaan van seksuele relaties negatief beïnvloedt, maar dat de impact hiervan aanzienlijk verschillend was voor mannen en vrouwen.

In **hoofdstuk 4** wordt een unieke studie over de genderidentiteit ontwikkeling bij kinderen, adolescenten en volwassen patiënten beschreven. In het hoofdstuk wordt eerst uitgebreid ingegaan op de methodologische aspecten en het onderzoek verricht naar de psychometrische eigenschappen van de gebruikte vragenlijsten. Vervolgens worden de bevindingen op de interviews en vragenlijsten gerapporteerd die verschillende aspecten van de

genderidentiteitsontwikkeling meten. Genderidentiteitsontwikkeling werd onderzocht in 60 kinderen (42 jongens, 18 meisjes), 24 adolescenten (15 jongens, 9 meisjes) en 34 volwassenen (19 mannen, 15 vrouwen) allen met DSD, en een even groot aantal gematchte controle personen. De meeste patiënten hadden nooit enige medische behandeling voorafgaand aan deze studie ondergaan. We zagen dat een opvallend hoog percentage patiënten hun sociale gender rol hadden veranderd: 6,7 % van de kinderen, 8,3 % van de adolescenten en 44,1 % onder volwassenen. Alle deze patiënten, met uitzondering van één, leefden eerst als vrouw en hadden op een gegeven moment besloten verder te willen leven als vrouw. Onder hen had 81 % een 46 XY karyogram en was er sprake van ondervirilisatie. Bij 14 % was de diagnose 46, XX CAH-SV gesteld. Alle patiënten hadden gedurende hun leven een aanzienlijke (lichamelijke) vermannelijking ondergaan. Er was verwarring over hun genderidentiteit, soms versterkt door het feit dat ook hun gedrag niet paste bij de gender waarin zij opgroeiden (kinderen die als meisjes opgroeiden maar leken in hun gedrag en interesses meer op jongetjes). Adolescente meisjes en vrouwen met DSD die wat mannelijker waren in gedrag en een stoer uiterlijk prefereerden ervoeren kritiek op hun levensstijl, hetgeen hen ongelukkig maakten. Het onderzoek toonde aan het verstandig is de medische follow-up gepaard te laten gaan met psychologische follow-up om hulp te kunnen bieden bij het omgaan met problemen op het gebied van gender identiteit en cross-gender gedrag.
In **hoofdstuk 5** presenteren we onze bevindingen betreffende emotionele en gedragsproblemen. Het onderzoek liet zien dat patiënten met DSD, in vergelijking met gezonde leeftijdsgenoten, zich vaker terugtrekken uit sociale contacten. Ook verdriet en depressieve klachten werden vaker door hen genoemd. Ernstiger vormen van depressie, waarbij behandeling moet worden overwogen, werden vaker gerapporteerd. Er was een verschil tussen mannen en vrouwen: mannen rapporteerden meer klachten op gebied van angst en depressie terwijl vrouwen zich vaker terugtrokken uit sociale contacten. Bij mannen werden de emotionele klachten vaak niet onderkend zodat er ook geen hulp werd gezocht of aangeboden. Bewust wording van het vaker voorkomen van emotionele problemen is een belangrijk om deze problemen tijdig te identificeren en hulp aan te bieden.

In **hoofdstuk 6** staat het onderzoek beschreven naar ervaringen van patiënten met sociale stigmatisering. Een deel van de chirurgische en hormonale

behandelingen zijn er op gericht om ambiguïteit van het lichaam te corrigeren. Dit wordt gedaan maatschappelijke stigmatisatie te voorkomen en er voor te zorgen dat patiënten optimale maatschappelijke kansen krijgen. Er zijn echter ook bezwaren: het zijn behandelingen die een grote impact hebben op het leven van het kind en het kind zelf is vaak nog te klein om te betrekken bij de beslissingen voor de behandelingen. Er is weinig onderzoek gedaan naar maatschappelijke stigmatisatie van DSD patiënten. Toch vragen bijna alle ouders van westerse patiënten om deze behandelingen.
De Indonesische patiënten van het Dr. Kariadi Ziekenhuis / Diponegoro Universiteit hadden weinig behandelingen ondergaan. Veel van hen hadden een ambigue lichaam. Daarom besloten we bij deze patiënten te onderzoeken of zij sociale stigmatisatie ervoeren en hoe stressvol dit voor hen was. We ontwikkelde een meetinstrument voor volwassenen en ouders; de Sociale Stigmatisatie Schaal voor DSD, met aparte versie voor volwassenen en ouders van kinderen en adolescenten. Daarnaast vroegen we patiënten of hun ouders hun antwoorden toe te lichten en voorbeelden te geven. Uit het onderzoek bleek dat patiënten sociale stigmatisatie ervoeren. Dat bleek zeker zo te zijn, met name patiënten die uiterlijke kenmerken van ambiguïteit hadden. Patiënten die ambigue kenmerken konden verbergen onder kleding kregen minder vaak te maken met sociale stigmatisatie. Stigmatisatie was stressvol en riepen veel emoties op. Deze patiënten werden vaak voor transgenders gehouden en ontmoetten veel hostiliteit. We hopen dat een betere bewustwording van het bestaan van DSD deze vooroordelen kan voorkomen. Daarnaast is het belangrijk de patiënt te ondersteunen en met hen copings strategieën te bespreken zodat zij vaardiger worden om voor zichzelf op te komen en een einde te maken aan de vijandigheden.

In **hoofdstuk 7** staan de bevindingen naar *health-related quality of life* (HRQoL). Op de vragenlijsten bleek dat DSD de kwaliteit van leven negatief beïnvloedde, met name bij kinderen en volwassenen. Kinderen vonden een slechtere aansluiting bij leeftijdsgenootjes en waren minder gelukkig dan controle kinderen (door de ouder en de kinderen zelf aangegeven). Volwassenen waren verdrietiger dan controle personen. Adolescenten en ouders rapporteerden geen invloed van DSD op hun kwaliteit van leven. De bevindingen op de kwaliteit van leven vragenlijsten kwamen overeen met de bevindingen op vragenlijsten voor gedrags- en emotionele problemen. Opnieuw is bewust

wording van de problematiek nodig om deze problemen tijdig te identificeren en hulp aan te bieden.

In hoofdstuk 8, worden de bevindingen van de verschillende onderzoeken besproken en in een bredere context geplaatst en aanbevelingen gegeven voor een geïntegreerde medische en psychologische aanpak voor behandeling zodat niet alleen de lichamelijke problematiek wordt behandeld, maar er ook oog is voor de maatschappelijke problemen die deze patiënten moeten overwinnen.

Rangkuman

Gangguan perkembangan organ reproduksi (dalam Bahasa Inggris disebut sebagai "*Disorders of sex development*" atau umumnya dan untuk selanjutnya disingkat dengan DSD) belum dikenal secara luas di masyarakat Indonesia, bahkan di kalangan praktisi kesehatan. Oleh karena itu, penanganan DSD di Indonesia menghadapi banyak rintangan disebabkan oleh kurangnya fasilitas diagnostik, pakar di bidang DSD, dan pengobatan medis, termasuk tindakan operatif. Disamping itu kesadaran masyarakat akan dampak DSD bagi penderita serta dampak yang muncul jika DSD terlambat ditangani sangatlah kurang. Pada tahun 1989, suatu tim multidisiplin untuk penanganan kasus-kasus DSD telah dibentuk, yakni Tim Penyesuaian Kelamin, yang merupakan kerjasama antara RS Dr. Kariadi dan Fakultas kedokteran Universitas Diponegoro (UNDIP) Semarang, Jawa Tengah (Indonesia) yang bertugas memberikan perawatan medis kepada pasien DSD. Tim Penyesuaian Kelamin ini seringkali dihadapkan pada pertanyaan-pertanyaan yang diajukan oleh pasien dan orangtuanya berkaitan dengan gender, antara lain mengenai penentuan jenis kelamin, kebingungan akan identitas gender, ketidakpuasan gender; persoalan dengan citra tubuh dan seksualitas; problem emosi, dan problem psikologis lainnya. Karena sebagian besar riset DSD di negara Barat dilakukan terhadap pasien yang telah ditangani sejak dini, kami seringkali mengalami kesulitan untuk memberikan informasi yang relevan dengan kondisi pasien kami.

Fokus riset kami adalah: "Apakah pasien DSD di Indonesia mengalami problem psikologis yang sama dengan pasien DSD di negara-negara Barat dan apakah dampak DSD terhadap perkembangan psikoseksual dan kesejahteraan psikologis pada pasien yang hanya sedikit mendapatkan bantuan medis?"

Penelitian psikologi yang dilakukan sejak tahun 2007 hingga 2013 ini merupakan bagian tak terpisahkan dari penelitian klinis yang mengkaji diagnosa 286 pasien DSD di Indonesia.

Bab 1 berisi pengantar mengenai DSD, terutama mengenai diagnosis DSD yang digunakan dalam penelitian ini, diikuti dengan gambaran umum mengenai pendekatan yang umumnya digunakan dalam menejemen pasien DSD di negara-negera Barat dan Timur, termasuk Indonesia (Semarang). Bab ini juga memaparkan secara garis besar aspek-aspek psikologis dari DSD, terutama dalam konteks diagnosis DSD yang dikaji dalam penelitian ini.

Bab 2 berisi informasi mengenai metode-metode yang digunakan dalam penelitian ini. Sebagian besar bahasan metodologi dipaparkan dalam bab 3-7, sehingga bab ini hanya dikhususkan pada aspek metodologi yang belum dijelaskan dalam bab-bab tersebut, termasuk antara lain konstruksi dan validasi skala serta hambatan metodologis yang dihadapi dalam melakukan suatu riset psikologi di Indonesia dengan menggunakan kelompok perlakuan dan kontrol.

Pada bab 3, kami paparkan temuan kami dalam riset yang melibatkan 34 pasien dewasa yang menderita DSD. Dalam hal seksualitas, fungsi seksual laki-lai dan perempuan, citra tubuh, distres seksual pada perempuan, dan orientasi seksual dikaji dalam penelitian ini. Data yang diperoleh menunjukkan bahwa pasien dewasa merasa tidak puas dengan bagian tubuh yang berkaitan dengan seks, seperti kelamin, buah dada, bulu wajah tetapi tidak demikian dengan bagian tubuh lainnya yang tidak berkaitan dengan seks, seperti mata, rambut, dan sebagainya. Dalam hal fungsi seksual, sebagian besar pasien wanita merasa tertekan dengan seksualitasnya. Perempuan dewasa penderita DSD menarik diri dari hubungan lawan jenis dan dari menghindarkan diri dari relasi cinta lawan jenis (pacaran). Dibanding perempuan, pasien laki-laki memiliki lebih banyak pengalaman dalam hal relasi dengan lawan jenis; mereka lebih cenderung ingin memiliki pasangan dan hubungan lawan jenis (pacaran), serta lebih banyak pasien laki-laki daripada perempuan yang menikah. Sebagian besar pasien dewasa yang diteliti, memilih atau tertarik secara seksual pada pasangan yang berlawanan gender dengan dirinya. Sebagian kecil pasien mengaku tertarik secara seksual pada orang dengan gender yang sama dengan dirinya. Temuan kami juga menunjukkan bahwa pasien dewasa, baik laki-laki maupun perempuan, khawatir dengan persoalan ketidaksuburan (infertilitas). Dilema untuk terbuka kepada orang lain atau pasangan mengenai kondisi DSDnya, pernikahan atau pasangan, dan ketakutan ditinggalkan atau ditolak pasangan merupakan persoalan-persoalan yang lebih sering ditemukan pada pasien perempuan daripada laki-laki. Kami menyimpulkan bahwa DSD berdampak besar bagi seksualitas pasien. Dampak yang ditimbulkannya berbeda pada laki-laki dan perempuan seiring dengan perbedaan tuntutal sosial pada laki-laki dan perempuan.

Dalam bab 4, kami melaporkan studi yang unik mengenai perkembangan gender pada pasien anak-anak, remaja, dan dewasa yang menderita DSD. Kami meneliti

identitas gender dan peran jenis gender pada 118 pasien Indonesian (76 laki-laki, 41 perempuan) dengan berbagai jenis diagnosa DSD dan membandingkan hasilnya dengan 118 subjek kontrol yang dipasangkan berdasarkan gender, umur, dan area tempat tinggal (desa, kota kecil, atau kota besar). Pada bagian pertama, kami laporkan aspek metodologi pengukuran, seperti penerjemahan alat ukur, adaptasi skala, dan asesmen kualitas psikometrik dari skala yang telah diterjemahkan. Pada bagian ke dua, kami melaporkan perkembangan gender pada 60 pasien DSD anak (42 laki-laki, 18 perempuan), 24 remaja (15 laki-laki, 9 perempuan), dan 34 dewasa (19 laki-laki, 15 perempuan). Sebagian besar pasien hanya menerima sedikit perhatian medis atau belum pernah menerima pengobatan media, sebelum pengambilan data psikologis ini. Kami menemukan sejumlah pasien, dalam persentase yang sangat tinggi, yang telah berubah gender: 6.7% di kalangan pasien anak-anak, 8.3% di kalangan pasien remaja, dan 44.1% di kalangan pasien dewasa. Kecuali satu orang, semua pasien tersebut berganti gender dari perempuan menjadi laki-laki. 81% diantaranya memiliki karyotipe 46,XY dan mengalami demaskulinisasi , sedangkan sisanya (19%) memiliki diagnosis 46,XX CAH-SV (hiperplasia adrenal kongenital tipe virilisasi simpel). Tubuh mereka mengalami maskulinisasi yang sangat signifikan. Kebingungan akan identitas gender dan perilaku berlawanan gender lebih sering dijumpai pada pasien anak-anak yang dibesarkan sebagai perempuan daripada pasien DSD anak yang dibesarkan sebagai laki-laki. Pasien DSD remaja dan dewasa yang dibesarkan sebagai perempuan juga lebih sering memiliki persoalan yang berkaitan dengan gender. Pemantauan lanjutan terhadap perkembangan gender pasien perlu dilakukan secara terpadu, melibatkan pemeriksaan klinis maupun psikologis, terutama menjelang pubertas dan masa dewasa.

Di **bab 5**, kami kemukakan temuan kami dari studi tentang problem emosi dan perilakuan pada pasien yang kami teliti. Dengan menggunakan kuesioner untuk pasien usia 11 tahun ke atas, kami mengevaluasi perilaku mereka. Orangtua juga mengisi kuesioner untuk anak-anak mereka yang berusia 6-18 tahun. Hasil temuan kami menunjukkan bawah pasien DSD lebih sering menarik diri dari lingkungan pergaulannya dan lebih sering merasa sedih dan tertekan dibandingkan subjek kontrol. Dibandingkan subjek kontrol, pasien dewasa laki-laki lebih sering mengalami kecemasan dan depresi, sementara pasien dewasa perempuan lebih sering menarik diri. Orangtua anak-anak melaporkan

persoalan yang sama dengan persoalan yang dikemukakan anaknya, namun di kalangan remaja tidaklah demikian. Tidak ada persoalan yang khas yang dilaporkan oleh remaja maupun orangtuanya.

Pada bab 6, kami sampaikan pengalaman pasien dalam hal stigmatisasi sosial. Lebih dari dua decade, kebijakan penanganan pasien DSD telah diperdebatkan, terutama karena tindakan operatif yang dilakukan dalam rangka pencegahan kerancuan tubuh dan kelamin. Tindakan operatif tersebut dilakukan untuk mencegah terjadinya stigmatisasi sosial yang terjadi dikarenakan penampilan yang aneh atau ganjil. Menariknya, belum ada penelitian yang secara khusus mengkaji stigmatisasi pada pasien DSD. Dalam kenyataannya, tidak ada literature yang mendukung praktek medis ini. Dalam penelitian ini, kami menggunakan metode kuantitatif dan kualitatif untuk mendapatkan gambaran mengena pengalaman pasien kami dalam hal stigmatisasi sosial. Kami menyusun skala rating untuk mengukur stigmatisasi sosial. Hasil temuan kami menunjukkan bahwa pasien yang memiliki karakteristik DSD yang mudah dikenali orang awam lebih sering mengalami stigmatisasi sosial dibanding pasien yang karakteristik DSD-nya tidak tampak mata atau dapat disembunyikan dibalik pakaian yang dikenakannya. Semakin sering stigmatisasi sosial yang dialami, semakin tinggi stress yang ditimbulkan oleh pengalaman tersebut. Pasien dengan karateristik DSD yang mudah dikenali harus menghadapi reaksi sosial terhadap DSD. Pasien dengan karakteristik DSD yang dapat disembunyikan dapat mengantisipasi dan mencegah agar DSD-nya tidak diketahui oleh orang lain.

Di bab 7, kami mengkaji sejauhmana DSD berdampak pada kualitas hidup penderitanya. Data yang kami peroleh dari subjek anak-anak menunjukkan bahwa DSD mempengaruhi fungsi sosial anak. Pasien anak mengalami kesulitan bergaul dengan anak-anak atau orang lain dalam lingkungan pergaulannya. Orangtua mereka juga melaporkan bahwa mereka kurang bahagia. Pasien dewasa menyatakan lebih sering merasa depresif atau tertekan. Sebaliknya, pasien remaja maupun orangtuanya tidak menunjukkan adanya tanda-tanda problem emosi maupun perilaku. Dengan demikian data yang kami peroleh dari studi kualitas hidup yang berkaitan dengan kesehatan (*health related quality of life* atau disingkat HRQoL) selaras dengan temuan kami dalam penelitian mengenai problem emosi dan perilaku serta temuan kami mengenai distres seksual.

Di bab 8, semua temuan dari studi-studi yang telah kami paparkan sebelumnya akan dibahas dalam konteks yang lebih luas. Rekomendasi disusun sebagai pendekatan terpadu terhadap persoalan klinis dan psikologis. Pasien DSD tidak hanya menghadapi persoalan somatis saja, namun ia juga harus bergelut dengan banyak persoalan psikologis. Pasien dapat mengambil manfaat dari pengetahuan dan pengalaman psikolog dalam menerima penyakitnya dan dalam menghadapi persoalan sensitif lainnya, misalnya ketika diamati atau dikucilkan. Karena persoalan psikologis ini berkaitan erat dengan aspek medis, penanganan terbaik bagi pasien DSD akan dapat dicapai melalui kolaborasi antara dokter dan psikolog.

Appendices

About the author

PhD portfolio

Acknowledgements

About the author

Annastasia Ediati was born on September 13, 1973 in Sragen, Central Java, Indonesia. She went to study psychology at the Faculty of Psychology, Gadjah Mada University (UGM), Yogyakarta between 1991 and 1997. Then she took professional program to become a psychologist at the Faculty of Psychology-UGM and graduated at 1999. Before graduated as a psychologist, she passed the selection to be a lecturer at the Faculty of Psychology, Diponegoro University (UNDIP), where she works until now. In 2001 she received STUNED scholarship to pursue a master program on the Human Resource Development at the Faculty of Educational Science and Technology, University of Twente, the Netherlands. Since 2006, apart from her main duties as lecturer at the Faculty of Psychology-UNDIP, she has been involved in a multidisciplinary team to provide care for patients with DSD that were referred to the Sexual Adjustment Team (SAT) from the Dr. Kariadi Hospital and Faculty of Medicine, Diponegoro University. Her main responsibility was to conduct psychological assessment and counseling to patients with disorders of sex development and their parents. Following her involvement in the SAT, she also involved as researcher in the Center for Biomedical Research (CEBIOR), Faculty of Medicine-UNDIP where she began to expand her interests on psychological aspect of genetic-related disease. Before leaving to Rotterdam for her Phd program, she also involved in teaching medical doctors –students of the genetic counseling master program in UNDIP- about the psychological aspect of DSD. She is married with Justinus Badiaraja Simanullang in December 27th, 2011 and will leave together in Semarang, Central Java as she will continue her work at the Diponegoro University.

PhD Portofolio

Name of PhD researcher:	: **Annastasia Ediati**
PhD period:	: September 2010 – January 2014
Promotors:	: Prof.dr. S.L.S Drop Prof.dr. S.M.H. Faradz
Co-promotors:	: Dr. A.B. Dessens Dr. E. Birnie

Description	Year
General courses	
- Basic SPSS	2011
- Biomedical English Writing and Communication	2012
Seminars and workshop	
- I-DSD workshop on e-learning	2013
- Symposium on "Disorders of Sex Development: a new paradigm?" Jakarta, Indonesia	2011
- PhD day of the Erasmus-MC	2011
Presentations	
- 4th International Symposium of DSD, Glasgow, UK (Oral)	2013
- Psychologist Research Meeting, Sophia Children Hospital (Oral)	2012, 2013
- Indonesian Student Association (PPI) Rotterdam (Oral)	2013
- Sophia Research Day – 150th anniversary of Sophia Children Hospital (Poster)	2013
- DSD symposium, Erasmus-MC (Oral)	2012
- 2nd International seminar and workshop on DSD, Semarang, Indonesia (Oral)	2012
- 1st international conference of Paediatric Psychology Network (PPN) UK & NL Oxford, UK (Poster)	2012
- 38th meeting of the International Academy of Sex Research (IASR), Lisbon, Portugal (Poster)	2012
- 37th meeting of International Academy of Sex Research (IASR) Los Angeles, USA (Poster)	2011

Other

- Applying research grants (by Erasmus MC Postdoc network)	2013
- Systematic Literature Retrieval using PubMed (by Medical Library)	2012
- Systematic Literature Retrieval using Medline/ PsycInfo (by Medical Library)	2012

Grant/reward

- Runner-up Best oral presenter at the 4th International Symposium of DSD, Glasgow, UK	2013
- Travel grant from the *Erasmus Trustfonds* to present at the 37th meeting of International Academy of Sex Research (IASR) Los Angeles, US	2011
- DIKTI scholarship from the Directorate of Higher Education, Ministry of Education and Culture, Indonesia	2010

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"In the long history of humankind (and animal kind, too) those who learned to collaborate and improvise most effectively have prevailed" - Charles Darwin

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List of Publications

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A Ediati, SMH Faradz, GHW Verrips, AZ Juniarto, SLS Drop, & AB Dessens. Health-related quality of life in Indonesian children, adolescents, and adult patients with disorders of sex development. *Submitted.*

A Ediati, AZ Juniarto, E Birnie, J Okkerse, A de la Croix, SLS Drop, SMH Faradz, & AB Dessens. Social stigmatization in Indonesian patients with disorders of sex development. *In preparation*.

AZ Juniarto, A Ediati, YG van der Zwan, LHJ Looijenga, FH de Jong, AB Dessens, SLS Drop, & SMH Faradz. (2013). Virilization due to androgen hypersecretion in a patient with an ovarian Leydig cell tumor: diagnostic and psychosocial implications. *Acta Medica Indonesiana*, 45 (2), 130-135.

TI Winarni, FEP Mundhofir, A Ediati, W Nillesen, HG Yntema, BCJ Hamel, SMH Faradz, & RJ Hagerman. (2013). The Fragile X-associated Tremor Ataxia Syndrome (FXTAS) in rural Indonesia. *Clinical genetics*, 83 (3), 263-268.

CG Widayanti, A Ediati, M Tamam, SMH Faradz, EA Sistermans, & AMC Plass. (2011). Feasibility of Preconception Screening for Thalassemia in Indonesia: Exploring the Opinion of Javanese Mothers. *Ethnicity & Health*, 16, (4-5), 483-499.

Gunungan is a puppet (wayang) that shaped like a mountain. At the front of the mountain, there is a gate with two giants as the guardians. Gunungan also known as the three of life, with many animals or fantastic creatures are depicted: a tiger, a bison, peacocks, birds, dragons. Gunungan represents the world and its content. During the puppet performance, gunungan is used to mark the beginning or the end of the story, or to signal between the scenes.

Health-related quality of life in Indonesian children, adolescents, and adult patients with disorders of sex development

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GENERAL COMMENTS

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